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# Study of coronary artery disease risk factors and value of CRP in coronary risk determination in semi urban population of western U.P. India

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## Abstract

This study was conducted to identify the factors that increase the risk for coronary artery disease and is an extremely important area in health sciences. A total number of 300 patients (92% males and 8% females) were studied. They were divided into two groups, above 40 yrs and below 40 yrs of age.

In the first group (> 40 yrs.) total number of patients were 240 (80% of total 300 patients). Among 240 patients males were 216 (90 %) and females were 24 (10%). High cholesterol more than 200 mg /dl was present in 55% males and in 50 % females. High triglyceride >150 mg % was present in 50 % males and in 48 % female patients. High LDL was present in 30 % males and 25 % females. Low HDL was present in 50 % males and 45 % females.

In second group (<40 yrs), all patients were males. High cholesterol was present in 58 % of cases. high triglyceride in 60 % cases, low HDL in 50 %, and high LDL in 45 % . Smoking was present in 30 % cases .Hypertension was present in 35 % cases .Obesity was present in 40 % males and 45 % , females. Central obesity was present in 60 % males and 79 % females

Association of age, high LDL cholesterol, and hypertension, high triglyceride in males and central obesity in females were recorded with CAD patients.

In the younger patients dyslipidemia was more common. Inflammatory markers such as CRP has limited usefulness in the prediction of CAD events over and above conventional risk factors.

## Introduction

Coronary artery diseases (CAD) are the leading cause of morbidity and mortality world wide<sup>1</sup>. The effective control strategies and targeted management of high risk individuals have been contributed to fall in CAD in the several developed countries whereas increased coronary artery disease mortality is reported in developing countries due to increased life expectancy and altered life style and socioeconomic changes associated with urbanization.<sup>2</sup> Increase of approximately 82 % mortality and 89 %

morbidity due to coronary artery disease is anticipated in developing countries between 1990 and 2020<sup>3</sup> Cardiovascular disease contribution has increased from 25.5 % in 1990 to 30.2 % of all causes of mortality in India . Studies in urban population showed higher prevalence of hypertension, hypercholesterolemia, diabetes, sedentary life style and central obesity.

Angina pectoris (chest pain caused by insufficient blood supply of heart) and acute myocardial Infarction (heart attack) are the two most common features of CAD<sup>3</sup>.

Other features of CAD include coronary insufficiency (prolonged ischemic type chest pain accompanied by transient S-T segment and T wave change in the ECG) and sudden unexpected death (death within an hour of the onset of symptoms where no other disease can be accountable.)<sup>21</sup>.

Three major cardiovascular risk factors have been well established for many years.<sup>1</sup> and include hypercholesterolemia, hypertension and smoking.

A fourth major risk factor is diabetes mellitus.

There is now much interest in inflammatory risk factors, especially high sensitivity C-reactive protein (hsCRP)<sup>8</sup> and to a lesser extent Lipoprotein associated phospholipase A2 (Lp-PLA<sub>2</sub>)<sup>9</sup>

This study is aimed at discovering the relation between risk factors and CAD in the western U.P of India.

## Materials and methods

This study was conducted in the Department of Medicine, M.M.C. Muzaffarnagar, U.P. & SIMS, Hapur, UP. India between April 2006 and June 2010.

Total number of 300 patients of ischemic heart disease was studied.

Detailed interviews were performed with the help of questionnaire prepared

according to guidelines of WHO<sup>13</sup> and included age, sex, education, occupation, history of smoking, alcoholism.

Anthropometric components included height, weight; waist and hip circumference were measured. Body mass index (BMI) was calculated using formula weight (kg)/ height (m<sup>2</sup>). Blood pressure was recorded in right arm in sitting position after rest period of 5 minutes. Systolic blood pressure was measured at first appearance of sound and diastolic pressure was recorded at disappearance of the sound.

A resting 12 lead ECG was performed on all the persons. Minnesota coding was used to grade ECG.

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A fasting blood sample was collected after overnight fast of at least 10 hours for biochemical investigations and C reactive protein. The biochemical parameters were performed using enzymatic kits as per the following methods. Serum glucose (trinder, 1969) total cholesterol (Allain et al 1974) triglycerides (Fossati and prencipe, 1982) and HDL (Donald and smith 1985) .LDL and V.L.D.L were calculated.

Hypertension was diagnosed when blood pressure was >140/90 mm Hg (20T) BMI > 25 WHR (waist hip ratio) (male >0.9 and female >0.8) were

Considered as obesity and central obese. Diabetes was diagnosed if fasting

Glucose level was > 126 mg/dl.

Coronary artery disease was diagnosed based on history of myocardial infarction (MI) or ECG changes suggestive of ST-segment depression (Minnesota 4-1 to 4-2) or Q wave changes (Minnesota codes 1-1-1 to 1-1-7) T wave changes (Minnesota codes 5-1 to 5-3).

CRP measurement has been recommended for cardiovascular risk prediction. Three risk categories have been defined on the basis of CRP levels: low (< 1mg/ l) intermediate (1-3 mg/l) and high (>3 mg/l).

Levels above 10 mg /l were considered to represent an acute phase reaction in variety of cases. This included infection, necrosis, trauma, malignancy and inflammatory diseases.

However chronic forms of these diseases might result in milder elevation of CRP.

## RESULTS

A total number of 300 patients (92% males and 8% females) were studied. They were divided in two groups,

**Table 1:** Electrocardiographic criteria for coronary artery disease

Age group	Q wave	Q+ST	ST	T wave	Total
males					
<40	6 %	4%	10 %	1.5 %	
> 40	7 %	2%	5 %	1%	
females					
<40	2.5 %	2 %	70 %	15 %	
>40	3.5 %	3%	40%	60 %	

ST-T changes were more in females

**Table 2:** Dyslipidemia associated with CAD patients in age Group 1 (>40 yrs age)

Risk factor	males	females
Hypercholesterolemia > 200 mg/dl	55 %	50 %
Hypertriglyceridemia > 150 mg/dl	50 %	48 %
HDL < 40 mg/dl	50 %	45 %
LDL >150 mg/dl	30 %	25 %

Dyslipidemia was more common in males above the age of 40 years

**Table 3:** Dyslipidemia associated with CAD patients in age Group 2- (<40 yrs age)

Risk factor	males
Hypercholesterolemia > 200 mg/dl	58 %
Hypertriglyceridemia > 150 mg/dl	60 %
HDL < 40 mg/dl	55%
LDL >150 mg/dl	45 %

Hypertriglyceridemia was more common in younger patients

**Table 4:** Association of smoking, hypertension, diabetes and obesity in coronary artery disease patients

Risk factors	Males	Females
Smoking + tobacco chewing	30 %	1 %
hypertension	35 %	32%
Diabetes	20 %	15%
Obesity	40 %	45 %
Central obesity	60 %	79 %

Central obesity was more common in females

**Table 5:** Association of CRP in CAD patients

Age group	Low <1 mg/L	Moderate 1-3 mg./L	High >3mg /L
< 40 years	66 %	33 %	01 %
> 40 years	68 %	30 %	02%

Low CRP levels were present in most of the cases in both the groups

above 40 yrs and below 40 yrs of age.

## Discussion

Our study demonstrates rising trends of CAD in India. Increased prevalence of CAD in semi urban population was attributed to genetic predisposition, thrombogenic tendency and altered life style..

The higher prevalence of CAD in males was observed in our study, Prevalence of Q waves,Q-ST waves was more in males than females and ST and T waves were more observed in females.

Major risk factors for coronary artery disease were Central obesity, low HDL, high cholesterol, high triglycerides, high LDL and hypertension.

In our study smoking was less in comparison to other Indian studies .It may be due to small sample or under reporting of smoking or may also be due to not performing S. nicotine assay to quantify smoking.

Hypertension, high cholesterol, high triglycerides, and high LDL were reported more in our study.

High prevalence of obesity and central obesity was observed in our study.

Hypertension and diabetes was more in males and obesity and central obesity were more in females.

Hypertension, diabetes and dyslipidemia were increased with age both in

males and females. CAD was more in females after age of 40 years.

CRP is a non-specific marker of inflammation which provides little incremental value to traditional cardiovascular risk factors.

Clinical importance of these risk factors needs to be tested in longitudinal Study.

## Conclusion

In this study dyslipidemia, obesity, central obesity and hypertension were found to be associated increased risk of CAD.

It may be possible that increased body mass index may be a contributory factor in higher prevalence of hypertension, high lipid levels and diabetes in the population studied.

It is known that individuals with a family history are more likely to develop CAD.

Currently much effort is taken to identify genes responsible for the risk factors and disease.

Treatment or control of risk factors can definitely reduce the morbidity and

mortality of coronary artery disease.

Determination of CRP provides little incremental value over traditional cardiovascular risk factors in the prediction of coronary artery disease. It is much less clinically significant than established risk factors such as being a

Smoker or having high cholesterol level. It is a non specific marker of simply being sick, and there is no evidence that lowering base line CRP will affect some one's health and till date no treatments that reduce or inhibit CRP are available.

## References

1. Murray CJL, Lopez AD. Alternative projections of mortality and disability by cause 1990-2020. Global burden of disease study. *Lancet* 1997;349:1498-504.
2. Reddy KS, YUSUF, S. Emerging epidemic of cardiovascular disease in developing country. *Circulation* 1998;97:596-601.
3. Ounpuu S, Negassa A, Yusuf S. Inter-heart: A global study of risk factors for acute myocardial infarction. *Am Heart J* 2001;141:711-21.
4. Janus ED, Postiglione A, Singh RB et al. On behalf of the council on arteriosclerosis of international society and federation of cardiology. Modernization of Asia. Implications of coronary heart disease. *Circulation* 1996;94:2671-73.
5. Bahl V, K, Prabhakaran D, Karthikeyan G. Coronary artery disease in Indians. *Indian Heart J* 2001;53:707-13.
6. Anand S, S, Yusuf S, Vuksan V, et al. Differences in risk factors atherosclerosis, and cardiovascular diseases between ethnic groups in Canada (LSHARE). *Lancet* 2000;356:279-84.
7. Bhatnagar D. The metabolic basis of increased coronary risk attributed to people from the Indian subcontinent. *Curr Sci* 1998; 74 : 1087 -94.
8. Gupta R, Gupta V.P. Meta-analysis of coronary artery disease prevention in India. *Indian heart journal* 1996 ;48:241 -45.
9. Mohan V, Deepa R, Rani SS, et al. Prevalence of coronary artery disease and its relationship to lipids in a selected population in South India. *J Am Coll Cardiol* .2001;38:682-87.
10. Beegom R, Singh RB, Prevalence of coronary heart disease and its risk factors in south and north India. *Acta Cardiol* 1995 ;50:227-40.
11. Usuf S, Ounpuu S. Tackling the growing South Asia (Editorial). *J. Am. Coll Cardiol*. 2001 ;38:688-89.
12. Rao GHR, White JG. Coronary artery disease. An overview of risk factors. *Indian heart journal* 1993 ;45:143-53.
13. Rose G, Blackburn, H, Gillum .RF, et al. *Cardiovascular survey Methods*, Geneva World health organization, 1982
14. The Seventh Report of the joint national committee on prevention, Detection, Evaluation and treatment of blood pressure. *JAMA* 2003;289:2560-72.
15. NCEP Expert panel on detection, Evaluation and treatment of high Blood cholesterol in adult's. *Circulation* 2002 ;17/24 :3145-21.
16. United nations Population division. World population prospects. The 2002 revision, volume II The sex and age distribution of population. United nations. Newyork, 2003 pp 492
17. Reddy KS. Cardiovascular diseases in India. *Wld Hlth stat Q* 1993;46: 101-107.
18. Enas EA, Yusuf S, Mehta JL. Prevalence of coronary heart disease In Asians. *Am.J. Cardiol*. 1992 ;70:945-49.
19. Sarvotham S.G, Berry JN. Prevalence of coronary heart disease in Urban population of northern India. *Circulation* 1968 ;37:839-46.
20. Gupta R, Prakash H, Majumdar S, et al. Prevalence of heart disease And coronary risk factors in an urban population of Rajasthan, India. *Indian heart journal* 2002 ;54:59 -66.
21. Friedman G D, Kannel WB, Dawber TR, et al. An evaluation of Of follow-up methods in the Framingham Heart Study. *Am J. public health* 1967;57:1015-24.

# Prevalence of anaemia among adolescent girls in urban areas of Kadapa, A.P.

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## Abstract

### Background

The prevalence of Anemia is disproportionately high in developing countries due to poverty, inadequate diet, certain diseases, pregnancy, lactation and poor access to health services. The world's adolescent population age 10-19 years estimated to stand more than 1 billion, yet adolescence remained a largely neglected, difficult to measure and hard to reach population in which the needs of adolescent girls, in particular are often ignored.

### Objectives

1. To know the prevalence of anaemia among adolescent girls. 2. To find the demographic profile among the adolescent anaemic girls.

### Methodology

The present cross sectional community based study was conducted in an urban field practice area of community medicine during the period of June 2008 to Nov 2008. A random sample of 248 girls participated and house to house survey conducted. Hemoglobin Estimation was done by Sahli's method. Diagnostic criteria for anaemia was Haemoglobin level < 12 gms for non pregnant women adolescent girls and < 11 gms for pregnant adolescent girls.

### Results

The prevalence of anemia was found to be 68.95%. A significant association of anemia was found with low socio-economic status ( $p < 0.05$ ). High prevalence of anaemia was observed in parents of truck, auto and laborers families and which was significant ( $P < 0.001$ ). Prevalence of anaemia more or less same in all the age groups of adolescent age in our study.

### Keywords

Age, Anthropometric measurements, BMI, Parents occupation, Socio economic status, marital status

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## Background

Nutritional anaemia is a disease syndrome caused by malnutrition in its widest sense (1). It has been defined by WHO as "a condition in which the haemoglobin content of blood is lower than normal as a result of a deficiency of one or more essential nutrients, regardless of the cause of such deficiency". Nutritional anaemia is a worldwide problem with the highest prevalence in developing countries. It is found especially among Adolescent girls, women of child-bearing age, young children and during pregnancy and lactation.

Iron deficiency can arise either due to inadequate intake or poor bio-availability of dietary iron or due to excessive losses of iron from the body. Although most habitual diets contain seemingly adequate amounts of iron, only a small amount (less than 5 per cent) is absorbed (2). This poor bioavailability is considered to be a major reason for the widespread iron deficiency (3). Women lose a considerable amount of iron especially during menstruation. Some of the other factors leading to anaemia are malaria and hookworm infestations.

Adolescence has been defined by the World Health Organization as the period of life spanning the ages between 10 to 19 years. (1) This is the formative period of life when the maximum amount of physical, psychological, and behavioral changes take place. This is a vulnerable period in the human life cycle for the development of nutritional anaemia, which has been constantly neglected by public health programs. Girls are more likely to be victim due to various reasons. Among adolescents, girls constitute a vulnerable group, particularly in developing countries when they are traditionally married at an early age and exposed to a greater risk of reproductive morbidity and mortality they are deprived of food & education the added burden of menstrual blood loss, normal/abnormal, precipitates the crisis too often.

In a family with limited resources, the female child is more likely to be neglected and is utilized as an extra working hand to carry out the household activities. For these reasons, we felt important to study adolescent girls with diminished iron stores. This study was planned to highlight the problem of anaemia in adolescent females and to study socio-demographic factors related to anaemia.

### Objectives

1. To know the prevalence of anaemia among adolescent girls.



2. How the nutritional status influencing the anaemia in adolescent girls.
3. To find the demographic profile among the adolescent anaemic girls.

## Materials and methods

The Urban Health and Training Center, Akkayapalli, Kadapa is an urban field practice area attached to the Department of Community Medicine, Rajiv Gandhi Institute of Medical Sciences, Kadapa. The present Cross sectional community based study was conducted at Akkayapalli area using the simple random sampling method. from among the beneficiary areas under this center. The population coverage of Urban Health Centre is about 27,568. Initially, a pilot study was conducted to pretest the proforma and to have a rough estimate of the prevalence of anaemia, the prevalence was found to be 50%. In this pilot study, prevalence was shown to be 50%, and allowable error taken as 15% and formulae used here is  $4PQ / L^2$ .

Where, P = prevalence of Anaemia (50%)

$$Q = 100 - P$$

$$L = \text{Allowable error (15\%)}$$

According to this formulae, the sample actually is 179 and additionally taken another 69 cases. Finally sample size in this study was 248. Nearly 08 cases were not participated in this study. A pilot study was conducted and tested and the actual study was started after making necessary corrections and advises in it. The study was approved by the ethical committee of the Rajiv Gandhi Institute of Medical Sciences, Kadapa. A house-to house survey was carried out by the investigator. After obtaining written informed consent from the head of the household, information about the socio-demographic characteristics was recorded in the predesigned, pretested proforma. This was followed by a clinical examination of the subject including height and weight. Socio-economic status (SES) was estimated according to a ration card verification issued by a Govt. of Andhra Pradesh. For hemoglobin estimation, 20 µl of capillary blood was taken in a hemoglobinometer pipette and transferred to a Hb diluting tube gently by immersing the tip in N/10 Hcl. Allowed 10 minutes, during this period Hb reacts with acid and gets converted into a dark brown pigment called acid haematin. Diluted the acid haematin with distilled water till it matches with colour of the standard coloured glass rods. Noted the reading in grams against his id. The next day, the results of the hematological investigations were conveyed to the subjects and those found to have anaemia were given appropriate treatment and advice regarding proper diet.

## Criteria for anaemia

Hb<12 gm% for nonpregnant adolescent, Hb<11 gm% for pregnant adolescent.<sup>(4)</sup>

## Statistical analyses

The statistical analyses were done using Chi-square test,

mean, Proportions etc. The help of a statistician was sought while analyzing the data.

## Results

Table-1 shows that the prevalence of Anaemia in adolescent girls was 68.95%, of which 76.4% were from

**Table 1: Age wise distribution of anaemia**

AGE	Anaemic < 12gm/dl	Non Anaemic	Total
10-12	54(65.85)	28(34.14)	82
13-15	65(76.47)	20(23.53)	85
16-19	52(64.20)	29 (35.80)	81
Total	171(68.95)	77(31.05)	248

$\chi^2=1.27$ , 1DF,  $P > 0.05$ , not significant.

**Table 2: Socio – economic status in relation to anaemia:**

Socio economic	Anaemic	Non Anaemic	Total
Below Poverty	95(75.4)	31(24.6)	126
Above Poverty	76(62.3)	46(32.7)	122
Line			
Total	171(68.95)	77(31.05)	248

$\chi^2 = 4.92$ , 1df,  $P < 0.025$ .

**Table 3: Occupation of father according to anaemia**

Occupation	Anaemic <12 gm /d1	Non Anaemic	Total
Father			
Auto, Truck Drivers Labour	40(75.47)	13(24.53)	53
Farmers	55(75.34)	18(24.65)	73
Teachers	31(52.54)	28(47.46)	59
Business men	45(71.43)	18(28.57)	63
Total	171(68.95)	77(31.05)	248

$\chi^2=30.31$ , 3df,  $P < 0.01$ .

the age group of 13-15 yrs and 65.8% were from the 10-12 yrs of age

Table-2 reveals that out of 171 anaemic adolescents, 75.4% (95) were from the below poverty line and only 62.3% (76) individuals from the above poverty line group. There was significant association was found between the below poverty line individuals and anaemia ( $P < 0.01$ )

Table-3 depicts that Out of 171 anaemic adolescent girls, about 75.4% were from the auto, truck drivers and labourer families. Nearly 75.3% were from farmers background and less number of anaemics (52.5%) from teacher families. Father occupation was significantly associated with anaemic condition ( $P < 0.01$ ).

Table-4 reveals that based on Anaemic girls and Body Mass Index, out of 171 anaemic girls, there were about < 18.5 BMI adolescent anaemic girls were -70.24% ,18.5-25 BMI anaemic girls were-68.1% (Normal) and >25 BMI anaemic girls were about 61.54% ( OverWeight). Though there is more number of anaemic persons in less than 25 BMI range

this association was not statistically significant ( $P>0.05$ ).

**Table 4: Body mass index in relation to anaemia**

Body Mass Index	Anaemic	Non Anaemic	Total
<18.5	99(70.24)	42(29.79)	141
18.5-25	64(68.09)	30(31.91)	94
>25	8(61.54)	5(38.46)	13
Total	171(68.95)	77(31.05)	248

**Table 5: Gradient of anaemia in the study population:**

Age	Mild 10-12	Moderate 7-10	Severe < 7	Total
10-12	12(22.22)	35(64.8)	7(12.96)	54
13-15	15(23.09)	47(72.3)	3(4.61)	65
16-19	22(42.30)	28(53.85)	2(3.85)	52
Total	49(28.65)	110(64.33)	12(7.02)	171

Table-5 shows that out of 171 adolescent anaemic individuals, majority (110) from moderate anaemic status, 49 anaemics from mild anaemic status and less (12) number of anaemics from severe anaemic condition.

## Discussion

The overall prevalence of anaemia was found to be 68.95%. Similar prevalence was reported by CMS Rawat et al. (12) at Meerut. A higher prevalence was noted by J Rajaratnam et al (16). The overall prevalence has increased from 74.2% (1998-99) to 79.2% (2005-06). Nagaland has the lowest prevalence (44.3%), Goa was the next (49.3%) followed by Mizoram (51.7%). Bihar had the highest prevalence (87.6%) followed closely by Rajasthan (85.1%), and Karnataka (82.7%). There are interstate differences in prevalence of anaemia that are perhaps attributable partly to differences in dietary intake and partly to access to health care (6). Toteja GS et al. (13) found 90.1% prevalence of anaemia among adolescent girls from 16 districts of India, with 7.1% having severe anemia. A significant association of the prevalence of anaemia with Occupational status of father reflects better awareness about the dietary intake of the children in the families and economic status directly proportional to the availability of quality of food in the families.

In the present study, out of 171 anaemic girls, there were about < 18.5 BMI adolescent anaemic girls were 70.24% ,18.5-25 BMI anaemic girls were 68.1% (Normal) and >25 BMI anaemic girls were about 61.54% ( Over Weight). Though there is more number of anaemic persons in less than 25 BMI range this association was not statistically significant ( $P>0.05$ ). Out of 171 adolescent anaemic individuals, majority 64.3% (110) from moderate anaemic status, (28.7%) 49 anaemics from mild anaemic status and 7% (12) less number of anaemics from severe anaemic condition. Bulliy G et al.(14) found 96.5% prevalence among non school going adolescent girls in three districts of Orissa, of which, 45.2%, 46.9% and 4.4% had mild,

moderate, and severe anaemia. They found significant association between Hb concentration and the different Occupations of father and low socio economic status ( $P<0.001$ ).

## Conclusions and recommendations

The overall prevalence of anaemia among adolescent girls was found to be 68.95%. It reflects the overall nutritional status of adolescent girls. A significant association was found between the anaemia and low socio economic status and low profile occupations of father. Hence there is a need to develop strategies for intensive adult education and improve the socio economic status of the population through poverty alleviation programmes. This should be supported by programme for the prevention of nutritional anaemia.

## References

1. WHO (1982), World Health statistics quarterly, 35:52.
2. Narsinga Rao , B.S. (1978), Indian Journal Medical Research No.58.
3. Srikantia, S.G.(1983), Proceed Nutritional Society of India No. 28, Page.7.
4. WHO, programming for adolescent health and development. WHO Tech Rep Ser No. 886, 1996, P.2
5. WHO, Nutritional anaemia report of a WHO scientific group, Geneva WHO, 1968.
6. Govt. of India (2008), Eleventh five year plan 2007-12), Vol II, Planning Commission, New Delhi.
7. De Maeyer EM. Preventing and controlling iron deficiency anaemia through primary health care. A guide for health administrator WHO; 1989.P.26.
8. Rana.T. Age at menarche –nutritional status & other associated factors in urban Hyderabad girls, Ph.D. Thesis submitted to national institute of nutrition, Hyderabad 1983.
9. ICMR Bulletin.A reappraisal of the iron status indicators .Vol 27.1997.P.1
10. World Health Organization. In: Lwanga SK, Lemeshow S, editors. Sample size determination in health: a practical manual. 1991.
11. World Health Organization. Manual of basic techniques for a health laboratory. 1980. P. 371-4.
12. Rawat CMS, Garg SK, Singh JV, Bhatnagar M, Chopra H, Bajai SK. Sociodemographic correlates of anaemia among adolescent girls in rural district of Meerut. Indian Pediatr 2000;37:532-6.
13. Toteja GS, Singh P, Dhillon BS, Saxena BN, Ahmed FU, Singh RP, et al. Prevalence of anaemia among pregnant women and adolescent girls in 16 districts of India. Food Nutr Bull 2006;27:311-5.
14. Bulliy G, Mallick G, Sethy GS, Kar SK. Haemoglobin status of non school going adolescent girls in three districts of Orissa, India. Int J Adolesc Med Health 2007;19: 395-406.
15. Khanduri U, Sharama A. Megaloblastic anaemia:

Prevalence and causative factors. Natl Med J India  
2007;20:172-5.  
16. Rajaratnam J, Abel R, Asokan JS, Jonathan P, Prevalence

of Anaemia in adolescent girls in rural districts of  
Meerut. Indian journal of Community Medicine 2001;  
26:173-5.

# Cardiovascular endurance [physical fitness index] and maximal aerobic capacity [VO<sub>2</sub> max] in young male wrestlers

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## Abstract

Aerobic capacity or Maximal oxygen uptake capacity (VO<sub>2</sub> max) has been widely considered to be reliable and valid measure of cardiorespiratory fitness. Persons possessing higher values of VO<sub>2</sub> max have the capacity to yield larger amounts of energy, and are capable of performing better in athletic and other field activities. Cardiac endurance as determined by Harvard Step test is one of the component of physical fitness which reflects the ability of heart, lungs and blood vessels to deliver oxygen to working muscles and tissues and ability of those muscles and tissues to utilize that oxygen. Present study was done to determine Cardiac endurance [Physical fitness index] and Maximal oxygen uptake among 60 young male wrestlers in the age group of 11-25 years. Results of the study revealed no significant change in Cardiac endurance and VO<sub>2</sub> max when different age group wrestlers were compared. However, VO<sub>2</sub> max was significantly increased with increased duration of training among 16-20 age group wrestlers. This study also reflects the influence of age and training among wrestlers of Indian population.

## Keywords

Cardiac endurance, Maximal aerobic capacity, Wrestlers.

## Introduction

Physical fitness acquired in youth and maintained throughout life by means of an appropriate pattern of a healthy life style, including habitual physical activity, is thought to have beneficial effects on cardiovascular, respiratory and locomotor systems as well as cell metabolism and body reactions in general.<sup>1</sup> It is well known that, the capacity to perform work is influenced by many factors such as physical fitness, socioeconomic status, cultural habits and proper scientific training<sup>2</sup>. With the development of sports and exercise physiology and ergonomics the Harvard step test has been given much attention to select highly physically active persons who will be capable of doing hard work so that they may be recruited in various sports and games, defensive services or appropriate industrial occupations. American Alliance for Health, Physical Education, Recreation and Dance [AAHPERD] recommends this test to study health related physical fitness programme in youth.<sup>3</sup> There are very studies available on normal exercise measurements in young wrestlers of Indian Population. Determination of

Maximal oxygen uptake [VO<sub>2</sub> max] is one of the important criteria to assess the oxygen transport system, or cardiopulmonary efficiency. Persons possessing higher value of VO<sub>2</sub> max have capacity to yield larger amounts of energy and are capable of performing better in athletic and other field activities.<sup>4</sup> Sufficient data are lacking in our country regarding the values of VO<sub>2</sub> max in various healthy population groups as well as sportsmen. The purpose of this study was to find out the physical fitness index [PFI] along with aerobic capacity [VO<sub>2</sub> max] among young wrestlers grouped by age and training duration.

## Methods

Study was done on 60 male wrestlers attending a wrestling training school at Youth Services and Sports Centre, Davangere. These wrestlers were in the age group of 11-25 years and were divided into 3 groups: Group I consisted of wrestlers in the age group of 11-15 years, group II in the age group of 16-20 years and group III in the age group of 21-25 years. Further, in each of these different age group wrestlers, Cardiac endurance [PFI scores] and Maximal aerobic capacity [VO<sub>2</sub> max] were compared depending on their duration of training. All the wrestlers were in good healthy state free from any cardio respiratory and musculoskeletal disorders.

Cardiovascular endurance was tested using Harvard Step test.<sup>5</sup> Each subject completed up and down task [24 cycles /min] on an 18 inch bench for 3 minutes duration. The Physical fitness index [PFI] score was calculated as follows.  
PFI = Duration of exercise in seconds X 100

$$5.5 \times \text{Pulse count (1-1.30 min. after exercise)}$$

Physical fitness index was graded as poor [<84], average [84-90], good [91-95], very good [96-100] and excellent [> 100].

The Queen's college step test (QST) which has been recommended as a valid and reliable indirect method for prediction of VO<sub>2</sub> max in this particular population was adopted in the present investigation.<sup>6</sup> In brief the step test was performed by using a stool of 16.25 inches (or 41.30 cm) height. Stepping was done for a total duration of 3 minutes at the rate of 24 cycles per minute which was set up by a metronome. After completing subject were asked to remain standing comfortably and carotid pulse rate was measured from fifth to twentieth second of the recovery period. This fifteen second pulse rate was converted into beats per minute and following equation was used to predict VO<sub>2</sub> max.

$VO_2 \text{ max (ml/kg/min)} = 111.33 - (0.42 \times \text{pulse rate in beats per min})$ .

Statistical analysis was done using one way ANOVA test and Tukey's test.

## Results

Table I shows Cardiac endurance and  $VO_2 \text{ max}$  in the age group of 11-15 years [n=22]. On comparing wrestlers with d" 1 year of training duration [n=13] with wrestlers of 2-3 years training duration [n=9], there was no statistically significant difference in Cardiac endurance and  $VO_2 \text{ max}$ .

Table II shows Cardiac endurance and  $VO_2 \text{ max}$  in the age group of 16-20 years [n=22]. Wrestlers were again divided into 3 groups with training duration d" 1 year [n=5], 2-3 years [n=6] and 4-5 years [n=11]. On comparing these

wrestlers with different training duration, there was significant increase in  $VO_2 \text{ max}$  among wrestlers with increased training duration when compared to wrestlers with lesser training duration. However such a difference was not noted in other age group wrestler's with different training duration. Cardiac endurance was insignificant when different trained wrestlers were compared in 16-20 year age group wrestlers.

Similarly, no statistical difference was noted among wrestlers in the age group 20-25 years [n=16] on comparing with different duration of training [Table 3] with respect to Cardiac endurance and  $VO_2 \text{ max}$ .

Table IV compares Cardiac endurance and  $VO_2 \text{ max}$  among wrestlers grouped only by age without considering duration of training. There was no significant change in

**Table 1:** Cardiac endurance [pfi scores] and maximal aerobic capacity [ $vo_2 \text{ max}$ ] in 11-15 year age group [group i] wrestlers with different duration of training.

Parameters	Training duration				P-value*.
	1 Year [n=11]		2-3 years [n=9]		
	Mean	S.D	Mean	S.D	
Cardiac endurance [Pfi scores]	95.66	8.18	98.39	16.88	0.61 NS
$VO_2 \text{ MAX (ml/kg/min)}$	45.16	10.39	48.61	6.51	0.39 NS

\*One way ANOVA test. S.D: Standard deviation.

**Table 2:** Cardiac endurance [pfi scores] and maximal aerobic capacity [ $vo_2 \text{ max}$ ] in 16-20 year age group wrestlers [group ii] with different duration of training.

Parameters	training duration						P-value*	Significant Pairs**
	1] 1 year [n=5]		2] 2-3 year [n=6]		3] 4-5 year [n=11]			
	Mean	S.D	Mean	S.D	Mean	S.D		
Cardiac endurance [pfi scores]	105.97	5.55	103.28	18.70	109.19	14.52	0.84 NS	-
$VO_2 \text{ MAX(ml/kg/min)}$	30.69	0.00	48.33	4.22	50.70	8.28	0.01 S	1&2, 1&3

\*One way ANOVA test. \*\* Tukey's test.

**Table 3:** Cardiac endurance [pfi scores] and maximal aerobic capacity [ $vo_2 \text{ max}$ ] in 20-25 year age group wrestlers [group iii] with different duration of training.

Parameters	training duration				P-value*.
	4-5 Years[n=4]		>5 years [n=12]		
	Mean	S.D	Mean	S.D	
Cardiac endurance [pfi scores]	96.51	14.34	108.49	20.67	0.30 NS
$VO_2 \text{ MAX(ml/kg/min)}$	51.69	9.35	54.21	10.31	0.67 NS

\*One way ANOVA test.

**Table 4:** Cardiac endurance [pfi scores] and maximal aerobic capacity [ $vo_2 \text{ max}$ ] in different age group wrestlers.

Parameters	age group in years						p value*	significant pairs**
	1] 11-15 YEARS		2] 16-20 YEARS		3] 21-26			
	S.D	Mean	S.D	Mean	S.D	Mean		
Cardiac endurance [pfi scores]	96.77	12.20	106.31	14.93	105.50	19.58	0.092 NS	-
$VO_2 \text{ MAX(ml/kg/min)}$	46.57	8.99	47.41	8.59	53.58	9.83	0.051 NS	-

\*One way ANOVA test. \*\* Tukey's test.

Cardiac endurance and VO<sub>2</sub> max when different age group wrestlers were compared.

## Discussion

Cardiovascular endurance is the ability of heart, lungs and blood vessels to deliver oxygen to working muscle and tissues as well as the ability of those muscles and tissues to utilize that oxygen. Maximal aerobic capacity [VO<sub>2</sub> max] is a measure of the functional limit of the cardiorespiratory system and single most valid index of maximal exercise capacity. Further, VO<sub>2</sub> max is useful when changes in maximal aerobic capacity of children are assessed during the period of pre-puberty to adolescence.<sup>7</sup>The higher values of VO<sub>2</sub> max in athletes are the result of training besides may be some genetic endowment in them.<sup>8</sup>Training increases VO<sub>2</sub> max by increasing the cardiac output secondary to high stroke volume and an increase in arterio-venous O<sub>2</sub> difference. It appears that, physical training increases VO<sub>2</sub> max by about 50 % due to increase in cardiac output and the rest 50% due to increased extraction of O<sub>2</sub> by working muscle which is reflected in increased arterio-venous O<sub>2</sub> difference.<sup>9,10,11</sup>It is also observed that persons who are engaged in regular endurance training would improve their VO<sub>2</sub> max than persons who are more sedentary.

The results of this study shows that cardiac endurance and VO<sub>2</sub> max when compared in different age group wrestlers does not showed any significant change [Table IV]. The study also revealed that in the same age group wrestlers when cardiac endurance and VO<sub>2</sub> max were compared with respect to duration of training there was no significant increase in these parameters with increase in duration of training except in the age group of 16-20 years age group where VO<sub>2</sub> max showed significant increase with increase in duration of training [Table I, II, III].

Cardiorespiratory function is critical to performance of many sports and physical activities. In endurance trained adult athletes, the cardiorespiratory system typically shows evidence of having undergone series of favorable adaptations.<sup>12</sup>which are thought to contribute to performance. These adaptations include left ventricular enlargement, chamber wall thickening, an increase in cardiac contractility, an increase in cardiac output and electrocardiographic changes.<sup>13,14</sup> However, there no data on endurance trained children and adolescents to inform scientists, coaches and athletes about the normal sequence of adaptive changes that manifest in adult athletes. Timing of cardiovascular adaptations in young people is of great interest across a range of issues, including athletic performance, talent identification, growth and development, and cardiovascular health in adulthood. Present study does not revealed significant changes in cardiac endurance and VO<sub>2</sub> max in different age group wrestlers who were in pre-adolescent and adolescent stages. The fact that cardiac endurance and VO<sub>2</sub> max does not reveal significant changes when these different age group wrestlers were compared by duration of training

suggests lack of proper training schedule and improper training techniques among these wrestlers.

There are three main hypothesis to explain the interactions of exercise training and cardiac structure and functions.<sup>15,16</sup> First exercise training is responsible for all of the changes. Alternatively some athletes may have pre-existing cardiac advantages and engage in self selection to endurance type activities. Third, cardiac profiles in athletes reflect combination of exercise training and pre-existing cardiac structure and function. To thoroughly test these three hypothesis would require extensive longitudinal studies. In the present study, an attempt was made to find out Cardiac endurance by Harvard step test and VO<sub>2</sub> max by Queen's college step test and also to draw observations on the effect of training on specific age group wrestlers on these parameters. However this warrants further studies using electrocardiography and echocardiography to study and compare cardiac structure and function.

Cardiovascular adaptations related to endurance training are well known among male adult athletes. During endurance training heart improves its ability to pump blood mainly by increasing stroke volume. This occurs because of increase in end-diastolic volume, Left ventricular volume and left ventricular muscle mass. Endurance training is thought to cause LV enlargement characterized both by dilatation due to increase in blood volume loads [pre-load] and by hypertrophy, in response to increased contractility and force of contraction [afterload]. These modes of cardiac enlargement are distinct from those occurring in heart failure, with endurance training being associated with improved systolic LV ejection.<sup>17</sup> rather than impaired left ventricular function that is characteristic of heart failure. Endurance – exercise training may increase pre-load by several mechanisms, including increases in circulating blood volume [Ricci et al 1982] or increased filling times at rest and submaximal exercise [manifested as lower heart rates] to lead to increased increased stroke volumes.

## References

1. Anderson Lange K and Rutenfranz J 1997. Physiological indices of physical performance capacity. In: Measurement in health promotion and promotion. WHO regional publication, European series, no.22, p124.
2. Dey SK, Sinha SK 1994. Effect of training on some physical and physiological profiles of young female volleyball players. *Ind J of Physiol and Allied Sci*; 48(2): 69-77.
3. Safrit MJ 1986. Introduction to measurements in physical education and exercise science (Times mirror edn) Mosby college Publishing; 250.
4. Taylor HL, Bushirk E, Henschel A 1955. Maximal oxygen intake as an objective measure of metabolic functions in man. *J Applied Physiol*; 8:73-80
5. Neisner JS, Laurie JA 1969. Human biology- A guide to field methods. 2<sup>nd</sup> edition, Oxford and Edinburgh;

Blackwell Scientific Publisher: 325-328.

6. Chatterjee S, Chatterjee P, Bandyopadhyay A 2001. Enumeration of validity for predicted VO<sub>2</sub> max by Queen's college step test in Bengalee boys. *Indian J Physiol and Allied sci* ;55:123-127.
7. Yamaji K 1992. Science of maximum oxygen uptake. Tokyo, 1<sup>st</sup> ed. Kyorin Shoin Publisher: pp 14-191.
8. Klissouras V 1973. Sport in the modern world-chances and problems .Springer -Verlag. Berlin, Heidelberg New York; 504.
9. Ekblom B 1969. Effect of physical training on oxygen transport system in man. *Acta physiol Scand*: 328.
10. Ekblom B, Astrand PO, Saltin B, Stenberg J, Walstrom B 1968. Effect of training on circulatory response to exercise. *J Appl Physiol*; 2:518.
11. Rowell LB 1971. Physiology of work capacity and fatigue. Springfield, Simmonsoned ;132-169.
12. Ikaheimo MJ, Palatsi IJ, Takkunen JT 1979. Non-invasive evaluation of the athletic heart: sprinters versus endurance runners. *Am J cardiol* 44:24-30.
13. Smith SA, Humphary RH, Wohlford DLF 1994. Myocardial adaptation and weight fluctuation in college wrestlers. *Int J Sport Med*; 15:70-73.
14. Stork T, Mockel M, Muller R 1992. Left ventricular filling behavior in ultra endurance and amateur athletes: a stress Doppler echo study. *Int J Sports Med*; 13:600-604.
15. Stolt A, Karjalaneinen J, Heinonen OJ, Kujalu UM 2000. Left ventricular mass, geometry and filling in elite female and male endurance athletes. *Scand J Med Sci Sports*; 10:28-32.
16. Klissouras V 1973. Sport in the modern world-chances and problems .Springer -Verlag. Berlin, Heidelberg New York; 504.
17. Giorgi D, Di Bello V, Bertini A, Talini E, Valenti G, Cioppi A, Precisi S, Pallini M, Moretti L, Caputo MT, Giusti 2000. Physiological cyclic variation of the myocardial integrated backscatter signal in athlete's heart. *Int J of Sports Med* 21:616-22.

# Role of ascorbic acid supplementation on prevention of olanzapine induced metabolic side effects in schizophrenic patients

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## Abstract

Schizophrenia is one of the most debilitating disorders with devastating effects on its victims and their families. Atypical antipsychotics (AAPs) because of their superior efficacy, reduced side effects, & better compliance, have rapidly become the mainstay of treatment. However, these AAPs have unique side effect profile like weight gain, hyperglycemia, and hyperlipidemia. Although preliminary data suggest benefit of vitamin C in improving the lipid and glucose dysregulation, whether vitamin C as an antioxidant has any effect on improving drug induced metabolic derangements has not been clarified yet. Therefore, this prospective clinical trial has been carried out to determine the impact of vitamin C as an antioxidant in modifying these parameters in schizophrenic patients. Among 30 newly diagnosed DSM-IV patients of schizophrenia enrolled, mean body weight, BMI, blood sugar, and lipid profile were significantly increased from baseline to 6 and 12 weeks after treatment with olanzapine ( $p < 0.001$ ). However, there were no statistically significant differences in these parameters between patients who received only olanzapine and those who received both olanzapine and vitamin C. Thus, vitamin C as an antioxidant does not modify the metabolic side effect profile of olanzapine.

## Keywords

Schizophrenia, Olanzapine, Vitamin C, blood sugar, Lipid Profile.

## Introduction

Schizophrenia is a disturbance that last for six months or longer, including at least one month of delusions, hallucinations, disorganized speech, grossly disorganized or catatonic behavior, or negative symptoms. It has devastating effects on both its victims and their families. Furthermore, it extracts enormous economic cost from the society.<sup>1</sup>

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Till recent times, conventional antipsychotic drugs dominated the treatment of schizophrenia. But, the key pharmacological property of all neuroleptics i.e. ability to block dopamine D<sub>2</sub> receptors has been proved to be responsible not only for the antipsychotic efficacy but also for most of their undesirable side effects. Therefore, the well established effectiveness of these drugs came to closing stages.<sup>1</sup> Later on, atypical antipsychotics (AAPs) like olanzapine, because of its superior efficacy, reduced side effects, and prospects of better compliance, has rapidly become the mainstay of treatment and the first line drug for the treatment of schizophrenia irrespective of its stages.<sup>1,2,3,4</sup>

However, it has been gradually noticed that these AAPs have unique side effect profile like possible association with weight gain, hyperglycemia, and hyperlipidemia.<sup>5,6,7,8</sup> Furthermore, some studies are available showing the therapeutic benefit of vitamin C in improving the lipid and glucose dysregulation.<sup>9,10</sup> But, whether vitamin C as an antioxidant has any effect on improving drug induced metabolic derangements has not been clarified yet.

Therefore, this prospective clinical trial has been carried out to determine the impact of vitamin C as an antioxidant in modifying these parameters in schizophrenic patients.

## Aims and objectives

To study the effects of antioxidant (vitamin C) on olanzapine induced weight gain, hyperglycemia, and hyperlipidemia in patients of schizophrenia.

## Material and methods

The present study was approved earlier by the Institutional Ethics Committee of Indira Gandhi Government Medical College, Nagpur. The study was carried out on 30 patients from July 2005 to July 2006. Patients were recruited from Psychiatry OPD, Indira Gandhi Government Medical College, Nagpur.

### Inclusion criteria

- √ Newly diagnosed DSM-IV patients of schizophrenia
- √ Patients of either sex between 18-60 years of age.

### Exclusion criteria

- √ Patients with history of taking antipsychotics before study.
- √ Patients with history of diabetes mellitus.



- √ Patients with history of hyperlipidemia
- √ Patients taking antidiabetic treatment.
- √ Patients taking cholesterol lowering drugs
- √ Patients with documented cardiovascular diseases.

At the level of significance  $\alpha = 5\%$  and power 90%, the sample size of 30 was calculated using pilot study data of 10 patients in each group. Drugs which were given:

1. Tablet Olanzapine 5 mg two times a day orally.
2. Tablet Vitamin C 500 mg two times a day orally.

### Study design

A prospective, randomized, parallel, open label clinical trial was conducted in psychiatry OPD and department of pharmacology IGGMC, Nagpur. Patients attending psychiatry OPD were screened by the psychiatrist. Those found meeting the inclusion criteria were briefed about the trial. Patient Information Sheets were given to all prospective participants. Written informed consent was obtained from each patient before enrollment in the study by explaining the nature of the study to the patients and their care taker or family members.

After initial screening, the data regarding age, sex, past medical history, family history, physical examination and clinical examination was recorded in the case report form. Patient's weight and height was measured at the time of enrollment in the study. Investigations like fasting blood sugar, serum cholesterol, serum triglyceride, serum VLDL, serum LDL, and serum HDL were carried out at baseline.

After baseline investigations, patients were given tablet olanzapine for a period of 6 weeks. All the patients were again asked to report in Psychiatry OPD at 6 weeks for first follow up.

After 6 weeks, patients were randomly divided into two groups, group A and group B, Patients belonging to Group A (n=15) were given tablet vitamin C 500 mg two times a day for 6 weeks, while tablet olanzapine started at the time of enrollment in the study (0 week) was continued in the same dose. The patients belonging group B (n=15) were not given tablet vitamin C, but tablet olanzapine started at the time of enrollment in the study (0 week) was continued in the same dose for 6 weeks. All the patients were again asked to report in Psychiatry OPD at 12 weeks for second follow up and all the investigations were again carried out at 12 weeks.

Psychiatric evaluation of the patients was done by the psychiatrist at each follow up. No other psychiatric drug therapy was given to patients during the study period except rescue medications like tablet/injection lorazepam, tablet trihexyphenidyl, tablet clonazepam were available for managing emergency and side effects if any. General clinical safety was monitored by vigilant follow-up of patients for treatment emergent adverse events, if any and recorded in the case report form. Body Mass Index was calculated by formula<sup>11</sup>: Body Mass Index = Body Weight (kg) / Height (m<sup>2</sup>)

Fasting blood sugar was quantitatively estimated by GOD/POD<sup>12</sup> method, serum Total Cholesterol, Serum Triglyceride,

and Serum High Density Lipoprotein (HDL) was quantitatively estimated using semi autoanalyser<sup>13,14,15</sup>.

### Estimation of serum very low density lipoprotein (vldl):<sup>16</sup>

$$\text{VLDL in mg/dL} = \text{Triglyceride in mg/dL} \div 5$$

### Estimation of serum low density lipoprotein (ldl):<sup>16</sup>

$$\text{LDL in mg/dL} = \text{Total Cholesterol in mg/dL} - (\text{High Density Lipoprotein in mg/dL} + \text{VLDL in mg/dL})$$

### Statistical analysis of data

Mean values of change in body weight, BMI, and BSL and lipid profile (at baseline, 6 weeks, and 12 weeks) were compared between two groups by using Unpaired 't' test and in the groups by Paired 't' test.  $P < 0.05$  was considered as statistically significant in all analysis

### Abbreviations

No./n – Number, SEM - Standard error of mean, BW - Body weight, BMI - Body Mass Index, BSL - Blood sugar level, TC -Total Cholesterol, TG-Triglyceride, VLDL-Very Low Density Lipoprotein, HDL-High Density Lipoprotein, LDL-Low Density Lipoprotein.

### Observations & results

Observations and results of the present study are as follows: -

Table 1 shows demographic characteristics of study patients at baseline. Altogether 30 patients, meeting the inclusion criteria were included in the study. The mean age was 25.30 years (age range 19-36 years).

**Table 1:** Demographic Characteristics of Schizophrenic Patients

Age (Years)	Sex	
	Male	Female
25.30 ± 0.823	11	19

All the parameters, bodyweight, BMI, blood sugar and lipid profile were within normal clinical ranges at baseline (Table 2).

As shown in table 3, mean body weight, BMI and blood sugar level were significantly increased from baseline to 6 weeks and 12 weeks in olanzapine group ( $p < 0.001$ ). Also, it was observed that, serum total cholesterol, triglyceride,

**Table 2:** Baseline Parameters of Schizophrenic Patients

Parameter	Olanzapine (n=30)
BW (kg)	51.03 ± 1.412
BMI (kg/m <sup>2</sup> )	19.43 ± 0.533
BSL (mg/dl)	87.30 ± 1.793
TC (mg/dl)	162.36 ± 2.999
TG (mg/dl)	120.53 ± 3.843
VLDL (mg/dl)	24.20 ± 0.788
HDL (mg/dl)	44.27 ± 0.472
LDL (mg/dl)	93.90 ± 3.158

Values are given as Mean ± S.E.M.

Table 3: Effects of Olanzapine on various parameters after 6 and 12 weeks

Parameters	Olanzapine (n=30)		
	Baseline	6 week	12 week
BW (kg)	51.03 ± 1.412	52.80 ± 1.440***	55.70 ± 1.410***
BMI (kg/m <sup>2</sup> )	19.43 ± 0.533	20.11 ± 0.552***	21.23 ± 0.560***
BSL (mg/dl)	87.30 ± 1.793	94.63 ± 1.830***	104.73 ± 1.850***
TC (mg/dl)	162.36 ± 2.999	175.43 ± 2.884***	184.20 ± 2.790***
TG (mg/dl)	120.53 ± 3.843	128.50 ± 3.215***	137.30 ± 3.475***
VLDL (mg/dl)	24.20 ± 0.788	25.66 ± 0.638***	27.43 ± 0.691***
HDL (mg/dl)	44.27 ± 0.472	42.33 ± 0.482***	40.30 ± 0.399***
LDL (mg/dl)	93.90 ± 3.158	107.43 ± 3.015***	116.47 ± 2.919***

Values are given as Mean ± S.E.M., \*\*\*p<0.001 versus baseline

VLDL, and LDL increased significantly after 6 and 12 weeks of treatment with olanzapine (p<0.001) while, HDL decreased significantly after 6 and 12 weeks of treatment (p <0.001).

Table 4 shows the effects of vitamin C as an antioxidant on mean changes in various parameters when it was supplemented to the patients on olanzapine after 6 weeks. It revealed that, there were no statistically significant differences in mean changes in mean body weight, BMI,

**Table 4:** Mean Changes in Various Parameters after Vitamin C Administration in Olanzapine Group

Parameter	Mean Change Between 6 and 12 weeks	
	Olanzapine (n=15)	Olanzapine with Vitamin C (n=15)
BW (kg)	2.80 ± 0.296	3.00 ± 0.169
BMI (kg/m <sup>2</sup> )	1.12 ± 0.130	1.12 ± 0.078
BSL (mg/dl)	9.33 ± 1.150	10.87 ± 1.477
TC (mg/dl)	8.47 ± 0.467	9.07 ± 1.149
TG (mg/dl)	9.07 ± 1.540	8.53 ± 1.736
VLDL (mg/dl)	1.80 ± 0.341	1.73 ± 0.345
HDL (mg/dl)	-1.64 ± 0.260	-2.40 ± 0.456
LDL (mg/dl)	8.33 ± 0.583	9.73 ± 1.209

Values are given as Mean ± S.E.M.

mean blood sugar and lipid profile between patients who received only olanzapine and those who received both olanzapine and vitamin C.

## Discussion

Although newer AAPs, like olanzapine are the drugs of first choice for schizophrenia because of improvement in negative symptoms and lack of extrapyramidal side effects<sup>1,17,18</sup>, they are not absolutely free from side effects. Probably, they may have certain effects on various metabolic parameters which in turn may cause morbidity and affect the drug compliance. But, whether vitamin C as an antioxidant has any effect on improving drug induced metabolic derangements has not been clarified yet. A total of 30 newly diagnosed patients of schizophrenia based on DSM-IV diagnostic criteria of schizophrenia were included in the study.

In the present study, olanzapine and risperidone both were associated with significantly elevated body weight and BMI at 6 and 12 weeks. Allison et al. (1999)<sup>19</sup>, Conley et al. (2001)<sup>20</sup>, Garyfallos et al. (2003)<sup>21</sup> also observed significant weight gain and increase in body mass index (BMI) after 8 weeks of treatment with olanzapine.

In the present study, mean blood sugar was also found to be significantly elevated after 6 and 12 weeks of treatment with olanzapine. Lindenmayer et al. (2003)<sup>22</sup> observed statistically significant increase in mean blood glucose level after 8 and 12 weeks of treatment with olanzapine. In the present study, serum total cholesterol, triglyceride, VLDL, and LDL after 6 and 12 weeks of treatment were found to be increased significantly in olanzapine group. Also, it was observed that, serum HDL after 6 and 12 weeks decreased significantly in olanzapine group. Koro et al. (2002)<sup>23</sup>, Lindenmayer et al. (2003)<sup>22</sup> observed that olanzapine use was associated with nearly five fold increase in odds of developing hyperlipidemia.

To assess whether vitamin C has any modulating effect on drug induced metabolic derangement, vitamin C was added after 6 weeks. The antioxidant property of vitamin C was assessed by evaluating the effects of vitamin C on mean changes in various parameters when it was given to the patients after 6 weeks compared to changes in patient who did not receive vitamin C.

It was revealed that there were no statistically significant differences in mean changes in body weight, BMI, blood glucose, and lipid profile between patients who received only olanzapine and those who received both olanzapine and vitamin C.

Simon et al. (1998)<sup>24</sup> observed that serum ascorbic acid level was independently associated with high-density lipoprotein cholesterol (HDL-C); each 1 mg/dl increase in serum ascorbic acid level (range 0.1 to 2.7 mg/dl) was associated with a 2 mg/dl increase in HDL-C level. Vinson et al. (1998)<sup>25</sup> in their study in hamsters observed that the citrus extract plus ascorbic acid synergistically caused a significant reduction of 77%, 66%, and 40% in plasma total cholesterol, LDL + VLDL, and triglycerides, respectively. But, when we assessed the effect of vitamin C supplementation on various metabolic parameters, we found no significant impact of vitamin C in decreasing

metabolic side effects of AAPs. This could explain that, although vitamin C is believed to improve symptoms of schizophrenia and decrease the blood glucose and lipid profile by its antioxidant action, it has not influenced the net metabolic side effect profile of AAPs in our study, probably the oxidant cause is not responsible for the olanzapine induced increase in blood glucose and lipid profile. Still, further studies are required to explore this effect of vitamin C on metabolic outcome of AAPs.

Although, significant efforts have been taken to control for potential confounders, these efforts are not full-proof. The duration of six weeks may not have been sufficient enough to allow for modifications in various parameters by vitamin C to occur.

## Conclusions

Thus, we reached to the conclusion that significant increase in body weight, BMI, blood sugar and lipid profile of the schizophrenic patient caused by treatment with olanzapine at 6 and 12 weeks is not prevented or decreased by treatment with vitamin C. Thus, vitamin C as an antioxidant does not modify the metabolic side effect profile of olanzapine.

## References

1. Stahl SM. Essential psychopharmacology neuroscientific basis and practical application. 2nd ed. Cambridge University Press; 2004.
2. American psychiatric association practice guidelines for the treatment of patients with schizophrenia. *Am J Psychiatry* 1997; 154:1-63.
3. Bhana N, Foster RH, Olney R, Plosker GL. Olanzapine: an updated review of its use in the management of schizophrenia. *Drugs* 2001; 61(10):111-61.
4. Lieberman JA. Atypical antipsychotic drugs as a first-line treatment of schizophrenia: a rational and hypothesis. *J Clin Psychiatry* 1996; 57(11):68-71.
5. Farewell WR, Stump TE, Wang J, Tafesse E, L'Italien GL, Tierney, WM. Weight gain and new onset diabetes associated with olanzapine and risperidone. *J Gen Intern Med* 2004; 19:1200-05.
6. Fuller MA, Shermock KM, Secic M, Grogg AL. Comparative study of development of diabetes mellitus in patients taking risperidone and olanzapine. *Pharmacotherapy* 2003; 23(8):1037-43.
7. Ganguli R, Brar JS, Ayrton Z. Weight gain over four months in schizophrenia patients: a comparison of olanzapine and risperidone. *Schizophrenia Research* 2001; 49:261-67.
8. Koro CE, Fedder DO, L'Italien GL, Weiss S, Magder LS, Kreyenbuhl J, et al. An assessment of the independent effects of olanzapine and risperidone exposure on the risk of hyperlipidemia in schizophrenia patients. *Arch Gen Psychiatry* 2002; 59:1021-26.
9. Dai S, McNeill JH. Ascorbic acid supplementation prevents hyperlipidemia and improves myocardial performance in streptozotocin-diabetic rats. *Diabetes Res Clin Pract* 1995; 27(1):11-18.
10. Vinson JA, Sheu-Ju Hu, Jan S, Stansk NM. A citrus extract plus ascorbic acid decreases lipids, lipid peroxides, lipoprotein oxidative susceptibility, and atherosclerosis in hypercholesterolemic hamsters *J Agri Food Chem* 1998; 46(4); 1453-59.
11. Flier JS, Flier EM. Obesity. In: Harrison's principles of internal medicine. 16th ed. Kasper DL, Braunwald E, Fauci AS, Hauser SL, Longo, DL, Jameson JL. editors, New York: McGraw Hill, 2005,1311-19.
12. Miskiewicz SJ. Quantitative estimation of glucose by GOD/POD method. *Clin Chem* 1973; 19:253-54.
13. Tarbutton PN, Gunter CR. Quantitative estimation of serum total cholesterol. *Clin Chem* 1974; 20:724-26.
14. Foosati P. Quantitative estimation of serum triglyceride. *Clin Chem* 1982; 28:2077-79.
15. Finley PR. Quantitative estimation of serum HDL cholesterol. *Clin Chem* 1978; 24:931-34.
16. Rifai N, Warnick GR. Lipids, lipoproteins, apolipoproteins, and other cardiovascular risk factors. In: Tietz textbook of clinical chemistry and molecular diagnostics. 4th ed. Burtis CA, Ashwood ER, Bruns DE editors, An Imprint of Elsevier, 2006:903-81.
17. Thara R, Padmavati R, Shrinivasan TN. Schizophrenia. *The British Journal of Psychiatry* 2004; 184:366-73.
18. Baldessarini RJ, Tarazi I. Pharmacotherapy of psychosis and mania. In: Goodman and Gilman's the pharmacological basis of therapeutics. 11th ed. Brunton LL, Lazo JS, Pasrker KL, editors, McGraw Hill, 2005, 1753-71.
19. Allison DB, Mentore JL, Heo M, Chandler LP, Cappelleri JC, Infante MC, et al. Antipsychotic induced weight gain: a comprehensive research synthesis. *Am J Psychiatry* 1999; 156:1686-95.
20. Conley RR, Mahmoud R. A randomized double blind study of risperidone and olanzapine in the treatment of schizophrenia or schizoaffective disorder. *Am J Psychiatry* 2001; 158:765-74.
21. Garyfallos G, Dimelis D, Kouniakakis P, Sidiropoulos N, Karastergiou A, Lavrentiadis G, et al. Olanzapine versus risperidone: weight gain and elevation of serum triglyceride levels. *J European Psychiatry* 2003; 18:320-21.
22. Lindenmayer JP, Czobar P, Volavka J, Citrome L, Sheitman B, McEvoy JP, et al. Changes in glucose and cholesterol levels in patients with schizophrenia treated with typical or atypical antipsychotics. *Am J Psychiatry* 2003; 160:290-96.
23. Koro CE, Fedder DO, L'Italien GL, Weiss S, Magder LS, Kreyenbuhl J, et al. An assessment of the independent effects of olanzapine and risperidone exposure on the risk of hyperlipidemia in schizophrenia patients. *Arch Gen Psychiatry* 2002; 59:1021-26.
24. Simon JA, Hudes ES. Relation of serum ascorbic acid to serum lipids and lipoproteins in US adults. *Journal of the American College of Nutrition* 1998; 17(3):250-

- 55.
25. Vinson JA, Sheu-Ju Hu, Jan S, Stansk NM. A citrus extract plus ascorbic acid decreases lipids, lipid peroxides, lipoprotein oxidative susceptibility, and atherosclerosis in hypercholesterolemic hamsters. *J Agri Food Chem* 1998; 46(4); 1453-59.

# Halitosis: A review

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## Abstract

Halitosis or bad breath is a problem faced by many and can limit their potential to even interact with the society in a positive manner. It is very subjective in that for many this malady is "A perception rather than a real thing, everybody's breath smells to a certain extent". However real halitosis is an unpleasant condition which creates huge embarrassment with potentially grave consequences. Most of the individuals suffering from halitosis seek help from general practitioners initially, not the dentist.

## Keywords

Halitosis, Odour, Oral hygiene

## Introduction

### Halitosis

(Latin term) Halitus- breathing, Osis- pathological alteration is known by many terminologies which include **oral** malodor, breath odour, mouth odour, foul breath, fege bosta, fetor oris, fetor ex ore, or most commonly bad breath.

Tonzetich (1977) defined the term "Halitosis" as an unpleasant breath arising from physical and pathological causes from oral and systemic sources. Carranza describes it as food odour emanating from the oral cavity<sup>3</sup>

### History

Ancient folk remedies abound which are still in use. The book of Genesis mentions laudanum (mastic), a resin derived from the Pistachio lentiscus tree, which has been used in Mediterranean countries for breath freshening for thousands of years. Other folk cures include parsley (Italy), cloves (Iraq), guava peels (Thailand) and eggshell (China).<sup>8</sup>

### Mechanism of Halitosis

The exact cause for halitosis has been under investigation by many investigators. The release of free thiol groups and volatile sulphides have been invariably pointed out by many authors, anaerobic activity of pathogens being a potential source of residual products resulting in Halitosis.

- Proteolysis of proteins → peptides → amino acids → free thiol groups & volatile sulphides.
- Results from any form of sepsis: Increased anaerobic

activity of pathogens (inc. Treponema denticola, P.Gingivalis and Bacteroides forsythus).<sup>3</sup>

## Classification

Dominic P. Lu, in 1982 gave an etiologic classification of this condition to help clinicians develop the diagnostic acumen to distinguish one type of halitosis from another. He divided Halitosis into the following categories.

- (1) Halitosis due to local factors of pathological origin.
- (2) Halitosis due to local factors of non pathological origin.
- (3) Halitosis due to systemic factors of pathologic origin.
- (4) Halitosis due to systemic factors of non pathologic origin.
- (5) Halitosis due to systemic administration of drugs.
- (6) Halitosis due to xerostomia.

Miyazaki and colleagues in 1999 has given a tentative classification of halitosis.

According to them, halitosis can be classified into:

- I. Genuine Halitosis.
  - A. Physiologic Halitosis.
  - B. Pathologic Halitosis
    - (i) Oral pathologic.
    - (ii) Extra oral pathologic.
- II. Pseudo halitosis
- III. Halitophobia.<sup>1</sup>

## Halitosis due to local factors

**Table 1: Local causes of halitosis**

### Mouth

- Poor oral hygiene.
- Food packing and stagnation.
- Chronic periodontal disease.
- Acute necrotizing ulcerative disease.
- Dry socket.
- Pericoronitis.
- Chronic dental sepsis.
- Infections.
- Malignant tumor.
- Hemorrhage

### Nose and pharynx

- Pharyngitis
- Tonsillitis
- Sinusitis (post nasal drip)
- Malignant tumors
- Foreign bodies.

## Halitosis due to systemic administration of drugs

### Halitosis due to systemic administration of drugs

Isosorbides  
Ethyl alcohol  
Chloral hydrates  
Medications containing iodine, such as iodinated glycerol, amylnitrite  
Antihistamines  
Antineoplastics  
Diuretics  
Phenothiazines and its derivatives  
Tranquilizers  
Amphetamines  
Dimethyl sulfoxide

Genuine halitosis is a term used when obvious malodor intensity is beyond socially acceptable level. Genuine halitosis is sub classified as physiologic halitosis and pathologic halitosis.<sup>11</sup>

#### (a) Physiologic halitosis:

Physiologic halitosis is the term used when malodor arises through the putrefactive process with in the oral cavity. Neither a specific disease nor pathologic condition that could cause halitosis is found. The origin of this type of malodor is mainly in the dorsoposterior region of the tongue. The temporary halitosis as a result of dietary factors (e.g. garlic bread) should be excluded.

#### (b) Pathologic halitosis:

Pathologic halitosis is categorized into oral pathologic and extra oral pathologic halitosis.

#### (i) Oral pathologic halitosis:

Halitosis is caused by disease, pathologic condition, or

malfunction of oral tissues. Halitosis is derived from the tongue coating modified by pathological condition (e.g., periodontal disease, xerostomia etc) is included in this type of halitosis.

#### (ii) Extra oral pathologic halitosis:

Malodor originates from nasal, paranasal and laryngeal regions. A malodor also may originate from pulmonary tracts or upper digestive tracts. Malodor can originate from disorders anywhere in the body where by the odour is blood borne and emitted via lungs (Diabetes mellitus, hepatic cirrhosis, uremia, internal bleeding etc).

#### (iii) Pseudo Halitosis:

Obvious malodor is not perceived by others. Although a patient stubbornly complains of the existence of his/her halitosis. Improvement of this condition is highly promising by explanation, counseling and simple treatment measures.

## Diagnosis

### Self diagnosis and home diagnosis

One popular home method to determine the presence of bad breath would be to lightly scrape the posterior back of the tongue with a plastic disposable spoon and to smell the drying residue.<sup>6</sup>

### Professional Diagnosis

1. **Halimeter:** a portable sulfide monitor used to test for levels of sulfur emissions (specifically, hydrogen sulfide) in the mouth air.
2. **Gas chromatography:** portable machines, such as the Oral Chroma, are currently being introduced. This technology is specifically designed to digitally measure molecular levels of the three major VSCs in a

## Halitosis Due To Systemic Factors of Pathologic Origin

Disease Entity	Characteristic of odors
Diabetes mellitus or impending diabetic coma	Acetone, fruity (not detectable in well controlled patients)
Liver failure (terminal stage)	Sweetish, musky feculent "amine" odor resembling a fresh cadaver, known as fetor hepaticas"
Acute rheumatic fever	Acid, sweet
Protocaval venous anasamosis	Fetor hepaticas but characteristically intermittent in nature for long period of time
Blood dyscrasias	Surgical extraction wound
Liver cirrhosis	Odour resembling decayed blood. Ammonia or urine
Uremia, kidney failure	Odour mainly due to xerostomia with poor oral hygiene and /or toxic waste by products accumulated in the body
Syphilis, exanthematous disease, granuloma venerum Internal hemorrhage Eosinophilic granuloma, Letterer - Siwe- disease. Hand Schuller Christian disease	Patients have typical foul breath of persons with fusospirochaetal stomatitis
Scurvy	Necrotic, putrefactive, extremely foul odor-resembling ANUG but much more intense & fetid.
Noma, developed from patients who are debilitated or undernourished	Patients have the typical foul breath of persons with fusospirochaetal stomatitis.

sample of mouth air (hydrogen sulfide, methyl mercaptan, and dimethyl sulfide)<sup>4</sup>

3. **BANA test:** this test is directed to find the salivary levels of an enzyme indicating the presence of certain halitosis-related bacteria
4. **â-galactosidase test:** salivary levels of this enzyme were found to be correlated with oral malodor

### Home care and treatment

1. Gently cleaning the tongue surface twice daily is the most effective way to keep bad breath in control; that can be achieved using a tongue cleaner or tongue brush/scrapper to wipe off the bacterial biofilm, debris and mucus.
2. Eating a healthy breakfast with rough foods helps clean the very back of the tongue.
3. Chewing gum: Since dry mouth can increase bacterial buildup and cause or worsen bad breath, chewing sugarless gum can help with the production of saliva, and thereby help to reduce bad breath. Chewing may help particularly when the mouth is dry, or when one cannot perform oral hygiene procedures after meals (especially those meals rich in protein).
4. Gargling right before bedtime with an effective mouthwash
5. Maintaining proper oral hygiene, including daily tongue cleaning, brushing, flossing, and periodic visits to dentists and hygienists.
6. Maintain water levels in the body by drinking several glasses of water a day.<sup>8,9</sup>

### Mouthwashes

Mouthwashes often contain antibacterial agents including cetylpyridinium chloride, chlorhexidine, zinc gluconate, essential oils, and chlorine dioxide. Zinc and chlorhexidine provide strong synergistic effect. Sugar also helps prevent bad breath. They may also contain alcohol, which is a drying agent. Rinses in this category include Listerine.<sup>9</sup>

### Conclusion

Although halitosis has a multifactorial etiology, local factors

play a major role. In most cases halitosis results from bacterial action and substances containing or capable of producing hydrogen sulphide, methyl mercaptan, dimethyl sulfide and dimethyl sulfide. Any measures that reduce these bacteria and substances will eliminate most cause of halitosis. Once these factors of a given case of halitosis and its distinct odour are ascertained, proper treatment can be readily rendered and prevention achieved.

### Reference

1. Dominic P "Halitosis: An etiologic classification a treatment approach and prevention". *Oral surg* 1982;54:521-52
2. Yaegaki K, Coil JM: Clinical application of a questionnaire for diagnosis and treatment of halitosis": *Quintessence Int* 1999; Vol 30:302-306.
3. Carranza and Newmann :*Clinical periodontology* "8<sup>th</sup> Edition, 1996
4. Murata T, Rahardjo A, Fujiyama Y, Yamaga T, Hanada M, Yaegaki K, Miyazaki H. Development of a compact and simple gas chromatography for oral malodor measurement. *J Periodontol.* 2006 Jul; 77(7):1142-7.
5. Bosy T, Kulkarni GV, Rosenberg M, McCulloch CA. Relationship of oral malodor to periodontitis: Evidence of independence in discrete subpopulations. *J Periodontol.* 1994 Jan; 65(1):37-46.
6. Rosenberg M. Clinical assessment of bad breath: current concepts. *J Am Dent Assoc.* 1996 Apr; 127(4):475-82.
7. Scully C, Rosenberg M. Halitosis. *Dent Update.* 2003 May; 30(4):205-10.
8. Tonzetich J. Production and origin of oral malodor: A review of mechanisms and methods of analysis. *J Periodontol.* 1977 Jan; 48(1):13-20..
9. Scully C. What to do about halitosis. *BMJ*:1994; 308:217-218
10. Ueno M, K Shinada. Clinical malodor measurement with a portable sulfide meter: *Oral Dis* 2008; 14:264-269.
11. Broek A, L Feenstra, Baat C. A review on current management of Halitosis. *Oral Dis*(2008); 14:30-39.

# Effect of alcoholic extract of *Withania somnifera* linn roots on reproductive organs in streptozotocin induced diabetic rats

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## Abstract

“Effect of alcoholic extract of *Withania somnifera* linn roots on reproductive organs in streptozotocin induced diabetic rats.”

*Withania somnifera* linn (WS) is a perennial herb used in various Ayurvedic treatment procedures. Its role over the reproductive system is less studied especially in the diabetic.

## Aim

1. To rule out the effect of WS alcoholic root extract over the weight of the reproductive organs of Streptozotocin induced diabetic male rats. 2. To rule out the plants ability to increase the sperm count.

## Material and methods

Twenty four adult male albino rats were grouped into four groups. Diabetes induced by injecting a single dose of Streptozotocin (50mg/kg BW) intraperitoneally. Insulin was given to one group with 5 units/Kg BW intraperitoneally for 30 days. Alcoholic root extract of WS (500mg/Kg) was given to another diabetic group orally for 30 days. Blood sugar, Body weight, Weight of Testes, Cauda epididymis and Caudal Sperm count was determined on 31<sup>st</sup> day. Data collected were statistically analysed using SPSS ver.15.0 software.

## Results

Statistically significant improvement in terms of testes weight and Caudal sperm count was obtained in WS treated diabetic rats than that of insulin treated.

## Conclusion

*Withania somnifera* root extracts had the potency to increase the reproductive efficiency of the diabetic rats.

## Keywords

Diabetes, testes weight, cauda epididymis.

## Introduction

Since time immemorial, many plants are known to have medicinal values not only in India but also in other countries. Popularly known as medicinal herbs, these plants are used in treating many ailments like Diabetes

mellitus (DM), Osteo-arthritis, Rheumatoid arthritis, bacterial and fungal infections and also as immunomodulators.<sup>[1,2,3,4]</sup> Herbal therapy gains the acknowledgment and advantage over modern allopathic medicines because it is less toxic and almost free from side effects.<sup>[2]</sup> As per the World ethanobotanical information, more than 800 herbal plants are recognized as safe and effective in treating DM<sup>[1,3]</sup> *Withania Somnifera* Linn (WS), popularly known as Ashwagandha in Sanskrit, is one such plant.

## Review of literature

WS is an erect, perennial shrub with ovate leaves, clusters of small, yellow flowers and ovoid red fruits at the nodes. It belongs to the Order Solanaceae. It is commonly known as Ashwagandha, Dhuppa, Indian ginseng, Winter cherry, Ajagandha, Kanaie Hindi and Sann Al Ferakh. It is a commonly used herb in Ayurvedic medicine. The chemical constituents of root of WS are Lactones in nature, the main one being Withanolides. The other alkaloids are sitoindosides, somnine, somniferine, somniferinine, pseudowithanine, tropine, pseudotropine, 3- $\alpha$ -gloyloxytropine, choline, cuscohygrine, isopelletierine, anaferine and anahyreine.<sup>[5]</sup>

The leaves and roots of WS are widely used in treating many ailments like tumors, tubercular glands and bacterial and fungal infections.<sup>[6,7,8,9]</sup> The immunomodulator effect of this plant has also been proved. It is considered as a general tonic to improve the health and longevity of life and used by athletes, aged persons and pregnant ladies to prevent diseases.<sup>[10]</sup> It is also proved as an anti-inflammatory and anti-stressor agent.<sup>[11,12]</sup>

The antidiabetic effect of this plant was also explored thoroughly.<sup>[3]</sup> In experimental diabetic-induced rats, insulin treatment was found to restore gonadotropin level, reproductive organ weight, sperm counts and motility and seminal fructose to a certain extent. However, prostatic weight and prostatic acid Phosphatase levels remained abnormal. Testosterone treatment restored the above mentioned parameters to control levels, with the exception of LH. When these rats were treated with insulin and testosterone together it seemed to have a synergistic effect on spermatogenesis.<sup>[13]</sup>

Studies done on human males showed that WS effectively reduced oxidative stress and improved the level of antioxidants. It was also shown to be effective in improving the semen quality by increasing the levels of Testosterone,



LH, FSH and PRL. [13]

However, the effect of WS on the reproductive organ weights, especially the testes and cauda epididymis and on sperm count in STZ induced diabetic rats was not very well documented/reported in the literature. Hence an attempt had been made to explore the effect of WS on these parameters.

## Objectives

To study the effects of alcoholic extract of WS roots on the weight of testis and cauda epididymis and sperm count male diabetic rats

## Materials & methods

### Extraction of WS

Roots of WS were dried in shade and the powdered. Ethanol (70%) extract of this powder was obtained by using Soxhlet apparatus. The yield of the final product during extraction procedure was 20% (w/w) in terms of dried starting material. The residue was stored in the refrigerator until further use.

### Fosage of WS

Saline was used as the vehicle in the study. The final product of WS extract was dissolved in saline at 10 g/100 ml. For experimental use, this preparation was administered orally at a dose of 500 mg/kg body weight. Induction of diabetes

A single dose of streptozotocin (STZ) injection of 50mg / Kg bodyweight was given intra peritoneally, to overnight fasted rats. Diabetes status (FBS ranging 126-200mg%) of the animal was confirmed after third day by measuring the fasting blood sugar level by using an Optium glucometer and is considered as day 1 for all the rats of different groups.

### Experimental animals

Highly inbred 24 male albino rats of Wistar strain were selected for the study. The rats were of same age (60 days old) weighing 180 to 200 g. All the animals were maintained under standard conditions. Food and water were available *ad libitum*. The rats were randomly divided into 4 equal groups viz,

**Group I** : Normal Control animals - treated with saline only

**Group II** : Diabetes induced animals – DM induced by an intraperitoneal injection of a single dose of STZ (50 mg/kg BW)

**Group III** : Insulin (long acting) treated Diabetic rats - (5 units/kg) intraperitoneally daily for 30 days after inducing diabetes

**Group IV** : WS treated Diabetic rats- (500 mg/kg BW) orally daily for 30 days after inducing diabetes

All the experimental procedures were carried out in the forenoon between 0800 hrs and 0900 hrs, after obtaining clearance from the institutional animal ethical committee. On 31<sup>st</sup> day, the body weight was determined as well as

blood sample was collected to estimate fasting blood sugar level. Animals were decapitated under mild ether anesthesia. Testes and CE were isolated and dry weight was determined. Caudal Sperm count was carried out by using improved Neubauer's counting chamber after staining with eosin yellow stain.

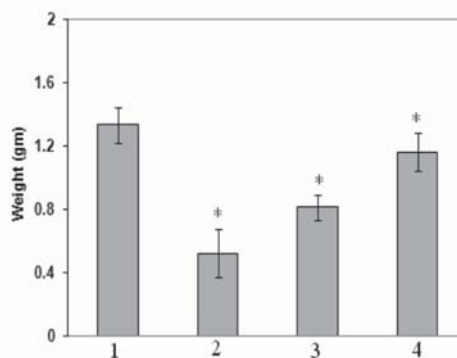
Data of results were analyzed by computer using Statistical software SPSS ver.15.0. One way analysis of Variance (ANOVA) was carried out followed by Tukey's multiple comparison tests to determine the significant differences between the groups. Statistical significance level was fixed at  $P < 0.05$

## Results

### Testes

There was a significant reduction in weight of the testis in diabetes induced rats ( $F = 56.187$ ;  $df = 3, 20$ ;  $P < 0.001$ ). Administration of insulin increased the weight significantly. However, increase in the testes weight by WS extract is more compared to that of insulin (Fig.1). Tukey's test revealed that the increase in the weight of the testis by WS is statistically significant compared to that of insulin.

**Fig. 1:** Weight of testes (Mean  $\pm$  SD)



1. Normal control                      2. Diabetes induced.  
3. Insulin treated                      4. WS treated

\* =  $p < 0.001$

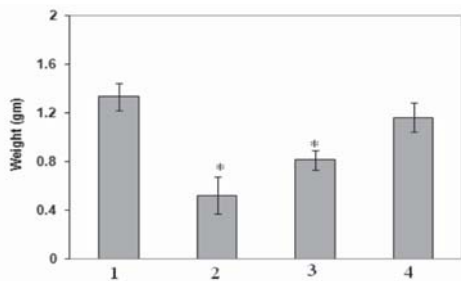
### Cauda epididymis

There was a significant reduction in the weight of CE in diabetes induced rats. ( $F = 64.27$ ;  $df ; 3,20$ ;  $p = 0.001$ ). Tukey's test also revealed that the administration of insulin improved the weight of CE significantly. WS extract also improved the weight of CE compared to that of diabetes group. But between insulin administered group and WS administered group there was no significant difference in improving the weight of CE. However, the improvement was better by WS than by insulin (Fig. 2)

### Sperm count

There was highly significant reduction in sperm count in

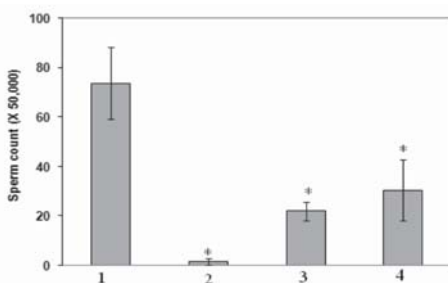
**Fig. 2:** Weight of Cauda epididymis(Mean  $\pm$  SD)



1. Normal control. 2 Diabetes induced.  
3. Insulin treated. 4. WS treated  
\* =  $p < 0.001$

diabetes induced rats. ( $F = 59.212$ ;  $df; 3, 20$ ;  $p < 0.001$ ). Both insulin and WS administration improved the sperm count significantly (Fig. 3). Tukey's test revealed that the increase was more significant in WS administration than in insulin administration.

**Fig. 3:** Caudal Sperm count (X 50000) (Mean  $\pm$  SD)



1. Normal control 2. Diabetes induced.  
3. Insulin treated. 4. WS treated  
\* =  $p < 0.001$

## Discussion

Few reports are available in support of the results obtained in this study regarding diabetic induced reduction in weight of testis and cauda epididymis and sperm count.<sup>[1,2]</sup> These effects are attributed to the diabetes induced alteration in neuroendocrine-reproductive axis which resulted in decrease in the levels of testosterone, LH and FSH.<sup>[14]</sup> This type of sexual dysfunction is noticed even in the diabetic subjects though the onset of the effects may vary depending upon the duration and severity of the ailment. After the onset of treatment these subjects showed improvement but normalcy was not reported.<sup>[14]</sup> The results of the present study revealed the normalizing activity of WS extract on diabetic induced changes in weight of testis and cauda epididymis and sperm count. The weight of testis and cauda epididymis and sperm count improved in insulin treated rats also. However, the improvement was better and almost nearer to basal level in rats treated with WS.

The exact mechanism of the normalizing actions of WS is not known because of the limitations of current literature.

One possible mechanism may be increased secretion of LH and FSH induced by WS as observed in infertile subjects treated with herbal preparations.<sup>[14]</sup>

The therapeutic use of WS for arthritis, rheumatism and Antistressor activity<sup>[15]</sup> is well established. However, in order to try this plant material for sexual dysfunction in diabetes, it is necessary to explore its normalizing actions on many other physiological changes induced by diabetes. It is also worthwhile to find out whether WS has direct actions on testis and other reproductive organs.

## References

1. Akhtar FM, Ali MR. Study of antidiabetic effect of a compound medicinal plant prescription in normal and diabetic rabbits. *Journal of Pakistan Medical Association* 1984; 34: 239 -244.
2. Brinker, F. *Herb contraindications and drug interactions*, 2<sup>nd</sup> Ed; Eclectic medical Publications Sandy, Or, USA, 1998 ;pp.36-82.
3. Rajangam Udayakumar, Sampath kasturirengan et al, Hypoglycemic and Hypolipidemic effects of Withania somnifera root and leaf extracts on Alloxan induced diabetic rats, *International journal of molecular sciences*, 2009, 10, 2367 – 2382.
4. Malik F, Kumar A, Bhushan S, et al, Immune modulation and apoptosis induction: Two sides of antitumoural activity of a standardised herbal formulation of Withania somnifera. *European Journal of Cancer* 2009, March (5).
5. Kulkarni S K, Ashish Dhir, Withania Somnifera- an Indian Ginseng, *Progress in Neuro-psycho Pharmacology & Biological psychiatry*, 2008 (32) 1093 -1105.
6. Singh N, Singh SP, Nath R et al. Prevention Urethane induced lung adenomas by Withania somnifera in albino mice. *International journal of crude drug research* 1986; 24: 90-100.
7. Devi PU, Sharada AC, Solomon FE, Kamath MS. In vivo growth inhibitory effect of Withania somnifera on a transplantable mouse tumor, Sarcoma 180. *Indian Journal of Experimental Biology* 1992 ;30: 169-172.
8. Devi P U, Sharada A C, Solomon F E. Anti-tumor and radiosensitising effects of Withania somnifera (Ashwagandha) on transplantable mouse tumor sarcoma 180. *Indian J. Exp. Biol.* 1993, 31, 607-611.
9. Sharad AC, Solomon FE, et al . Antitumor and radiosensitising effects of Withania A on mouse Ehrlich ascites carcinoma in vivo . *Acta Oncol* 1996; 35 : 95 - 100.
10. Chatterjee A, Pakrashi SC, *The Treatise on Indian Medicinal plants* 1995; 4: 208 -212.
11. Devi Pu, Sharada AC, Solomon FE. In vivo growth inhibitory and radiosensitizing effects of Withania Somnifera on mouse Ehrlich ascites carcinoma. *Cancer Lett* 1995; 95: 189-193.
12. Dadkar VN, Ranadive NU, Dhar HL, Evaluation of anti-

- stress activity of *Withania somnifera*, Indian journal of clinical Biochemistry 1987,2; 101 -108.
13. Ahmad MK, Mahdi AA, Shukla KK et al *Withania somnifera* improves semen quality by regulating reproductive hormone levels and oxidative stress in seminal plasma of infertile males . *Fertil Steril*- 2009 Jun 5. [Epub ahead of print]
  14. Seethalakshmi L, Menon M, Diamond D. The effect of streptozotocin-induced diabetes on the neuroendocrine-male reproductive tract axis of the adult rat. *J Urol*- 1987 Jul;138(1):190-4.
  15. Singh N, Nath R, Lata A et al *Withania somnifera*, a rejuvenating herbal drug which enhances survival during stress. *International journal of Crude drug research*, 1982; 20; 29-35.

# A profile of HIV positive antenatal women at PPTCT centre, Kadapa

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## Abstract

### Introduction

According to HIV surveillance by national AIDS control organization (NACO) in India, percentage of mother to child transmission cases among total AIDS cases is increasing year by year. HIV can be transmitted from mother to infant in 3 ways - Infection may occur in utero, the virus can be transmitted to the infant at the time of delivery or it can be transmitted through breast milk. Many social factors play a key role for increased incidence and prevalence of HIV to antenatal women.

### Objectives

1. To know the prevalence of HIV in antenatal women
2. To find the outcome of HIV positive pregnancies.
3. To identify the various social factors in HIV positive women.

### Methodology

A Hospital based cohort study at Rajiv Gandhi Institute of Medical Sciences, Kadapa, among PPTCT Centre attendees during the period of One year extends from October 2007 to September 2008. A total numbers of 4112 antenatal women were participated in this study and Oral interview with partially closed ended proforma was applied. The data thus obtained was subjected to analysis and results are presented.

### Results

About 4112 ANC are tested, out of which 56 (1.36%) were found to be positive. 51.78% of HIV positive ANC were observed in between age group of 15-24 years. 85.71% of HIV ANC were housewives. 96.42% of HIV+ ANC women were married. 75 % of HIV ANC delivered normally. Pregnancy wastage and IMR for HIV ANC is as high as 30%.27.5% of children delivered to HIV+ women are of low birth weight.

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## Conclusions

Low birth weight is an observed complication in HIV positive Antenatal case. A negative pregnancy outcome in the form of Pregnancy wastage and IMR is very high. This can be reduced some extent by Peer education, counseling, Proper antenatal checkups and good quality of delivery practices.

### Study variables

Age, marital status, Occupation, literacy, Type of Delivery, out come of Pregnancy, Birth weight, Spouse Counseling.

### Back ground

AIDS is the Burning problem of the world now. Out of the 4 major routes of transmission, "parent to child transmission" is most dangerous, because these children not only lose their parents, but also they are at the risk of poverty, neglect and early death. States where HIV prevalence in antenatal women is more than 1% are regarded as high prevalence states and Andhra Pradesh is one among them. The HIV infected pregnant women should be provided with the appropriate background for an informed reproductive choice, If she chooses MTP, safe MTP services must be provided to her. If she prefers to continue her pregnancy, she should be told about the risk of vertical transmission and her ante partum care should be tailored to her specific needs preferably with ample psychological support service to her. The knowledge of their HIV infection and will increase the opportunities for HIV infected pregnant women to prevent HIV transmission to their children. Ideally counseling and testing should precede pregnancy so that appropriate contraceptive advice can be given <sup>(1,2)</sup>.

Unfortunately many infected women do not seek or get prenatal care unit the 3<sup>rd</sup> trimester. Of those who are tested positive in early pregnancy and who choose to continue it, prenatal care will be somewhat altered by sero status and clinician's sensibility to a variety of the early symptoms of HIV disease. The keys to the appropriate care of the HIV infected women during pregnancy are optimal care of the pregnancy and optimal care of the HIV infection. General measures of proper diet, hygiene, rest etc. are to be strictly followed, nutritional counseling should be instituted if difficulty is encountered in maintaining appropriate weight gain. She must have enough sleep and must avoid stress and fatigue. Prevention of opportunistic infections

**Table 1:** Prevalence of HIV among antenatal women

No. attended	No. tested	No. counseled	No. positive	No. not counseled	Prevalence (%)
4786	4122	4109	56	13	1.36

is also a critical goal for the obstetrician (3).

An anti retroviral drug Nevirapine can only be used for the prevention of parent to child transmission of HIV and it should not be used for the treatment of HIV. For the pregnant woman one tablet of 200 mg of Nevirapine at the on set of labour and for the newborn 2mg/kg of oral suspension within 72 hrs of birth.

### Research question

What is the prevalence of HIV in antenatal women and the outcome of pregnancy in them?

### Objectives

- To know the prevalence of HIV in antenatal women
- To know the outcome of HIV positive pregnancies
- To know the various social factors in HIV positive women.

### Material and methods

**Study design:** A Hospital based cohort study

**Subjects:** All antenatal women coming to PPTCT centre at Rajiv Gandhi Institute of Medical Sciences(RIMS), kadapa

**Sample size:** All antenatal women (4112) coming to PPTCT between October-2007 to September-2008 subject to consent.

**Inclusion criteria:** Antenatal women who have registered at PPTCT and delivered between October-2007 to September-2008

**Exclusion criteria:** ANC registered before October-2007 and after September-2008

**Ethical considerations:** Informed consent is taken. Confidentiality regarding the HIV status and other issues is strictly followed

### Methodology

all the antenatal women attending PPTCT at RIMS, Kadapa in between October 2007 and September 2008 were included in the study. After informed consent, HIV screening was done. Those found to be positive were confirmed and studied in detail. Information regarding social factors was collected with the help of a questionnaire. HIV positive women were followed up to the delivery and information regarding the outcome of pregnancies was collected. The data thus obtained was subjected to analysis and results are presented.

### Results

About 4112 antenatal women were tested of which 56[1.36%] were found to be positive.

Most of the cases about 51.78% HIV+ANC were observed

**Table 2:** Socio-demographic variables of HIV positive antenatal cases

Age	No. of HIV+ ANC	% of HIV + ANC
<15 years	0	0
15-24 years	29	51.78%
25-34 years	26	46.42%
>35 year	01	1.78%
Total	56	100%
Marital Status		
Married	54	96.42
Single	-	-
Divorced	01	1.78
Widow	01	1.78
Total	56	100%
Occupation		
Daily wages	07	12.5
Business	-	-
House wife	48	85.71
Total	56	100
Literacy		
Illiterate	16	28.57
Primary school	27	48.21
Secondary school	07	12.5
College & above	06	10.71
Total	56	100%

in between the age group of 15-24 years.

96.42% of HIV+ANC women were married.

Occupations in relation to HIV+ANC women, about, 85.71% of HIV+ANC women were housewives. Literacy status in relation to HIV, about 48.21% were from primary school completed and less 10.71% no.of people from college and above completed ANC women.

Table 3 depicts that 75% of HIV+ANC were delivered

**Table 3:** Type of delivery among HIV+ANC women

Type of delivery	No. of HIV+ ANC women	%
Normal institutional	42	75
Normal home	02	3.57
Caesarian section	12	21.42
Total	56	100

normally in hospitals.

Table 4 reveals that 7 out of 46 live births died within 2 months of birth. Pregnancy wastage & IMR for HIV+ANC was as high as 30%

Table 5 reveals that 33.33% of children delivered to HIV+ women are of low birth weight.

Out of 56 HIV positive antenatal women, 53 spouses tested,

**Table 4:** Outcome of HIV positive ANC women:

Children status	No. of children	%
Live births	46	82.1
Still births	02	3.6
Abortion	08	14.3
Total	56	100

**Table 6:** Spouse status of HIV among HIV positive women:

	POSITIVE	NEGATIVE	TOTAL
Spouse	48	05	53
Child	04	12	16

of which 48 were found to be HIV positive and 16 children tested, of which 4 were found to be HIV positive.

## Discussion

The present study conducted at PPTCT centre of Rajiv Gandhi Institute of Medical Sciences, Kadapa during the period from October 2007 to September 2008. About 4786 ante natal women were visited to the PPTCT Centre, of which 4122 ANC women were undergone for HIV testing. Out of this, 56 women were found to be HIV positive and the antenatal prevalence reflecting 1.36%. This finding was observed in many high risk southern states like Maharashtra, Karnataka, Tamilnadu and about 18 districts of Andhra Pradesh (<sup>4</sup>).

Most of the cases about 51.78% HIV+ANC were observed in between the age group of 15-24 years. 96.42% of HIV+ANC women were married. No women conceived less than 15 years of age in this study and also above 35 years of age pregnant women was 1.78%. Occupations in relation to HIV+ANC women, about, 85.71% of HIV+ANC women were housewives and 12.5% were from daily wages and 1.78% from salaried women. Literacy status in relation to HIV, about 48.21% were from primary school completed and less 10.71% no.of people from college and above completed ANC women. This study findings were correlated with many other studies conducted in India and abroad. (<sup>5,6</sup>)

One of the important escalating finding in our study was about 75% of the HIV positive deliveries taken place as institutional normal deliveries and less proportion (21.42%) of the deliveries conducted through Caesarian Section. But, in relation to out come of the pregnancy, out of 56 ante natal women 46 gave live births, of which 7 died within 2 months of giving birth and 10 members were included as still births and abortions. Altogether ( 17 )Pregnancy wastage & IMR for HIV positive ANC was as high as 30%. Out of 56 ante natal women about 33% were low birth weight babies. All the HIV positive women and children received antiretroviral prophylaxis of Nevirapine during the onset of delivery for the mother and after the birth to the child. This has to be tracked for the confirmation of HIV positivity for the child and also efficacy of the Nevirapine therapy. (<sup>9,11,12</sup>)

## Conclusion

**Table 5:** Birth weight of child born to HIV+ANC women:

Weight	No. of children	%
<2.5 Kgs	16	33.33
>2.5 kgs	32	66.67
Total	48	100

Based on the above results in this study, Prevalence of HIV among antenatal women was 1.36%. Majority of Antenatal cases were between the age group of 15-24 years. Most of HIV+ANC women are married and are housewives. Low birth weight is an observed complication in HIV+ANC. A negative pregnancy outcome in the form of pregnancy wastage and IMR is very high. More than 90% of spouses of HIV+ANC women are found to be positive.

## References

1. UNAIDS REPORT-2005
2. National AIDS Control Programme – India Country Scenario an update 1996, page 30. NACO,Ministry of Health and Family Welfare, Government of India.
3. NACO, Training module on HIV Infection and AIDS for Medical Officers:Page No 112 to 115.
4. WHO (2004), World Health Report 2004, Changing history.
5. Abrams EJ, Myer L, Rosenfield A, El Sadr WM. Prevention of mother-to-child transmission services as a gateway to family-based human immunodeficiency virus care and treatment in resource-limited settings: rationale and international experiences. American Journal of Obstetrics and Gynecology 2007;197 (3) Suppl. 1:S101-S106.
6. Govt.of India (1999), The National Response to HIV/AIDS in India, National AIDS control Project phase –II, NACO, Ministry of Health and family welfare.
7. Little K, Newell ML, Luo C, Ngongo N, Borja MC, McDermott P. Estimating the number of vertically HIV-infected children eligible for antiretroviral treatment in resource-limited settings. International Journal of Epidemiology 2007;36(3):679-687.
8. Becquet R, Leroy V. The challenges of preventing mother-to-child transmission of HIV in Africa. Presse Medicale 2007;36 (12) Part 3:1947-1957.
9. Sinha G, Dyalchand A, Khale M, Kulkarni G, Vasudevan S, Bollinger RC. Low utilization of HIV testing during pregnancy - What are the barriers to HIV testing for women in rural India? Journal of Acquired Immune Deficiency Syndromes 2008;47(2):248-252.
10. WHO (2008), HIV situation in south east Asia, HIV Unit Department of Communicable Diseases, Regional office for south east asia.
11. CROI. Update on HIV infection and breastfeeding: Overview of the CROI 2008, Boston. 2008. Postnatal HIV transmission, infant outcomes and infant feeding practices.
12. Internet website: [www.naco.nic.in/vsnaco/indiascene/update](http://www.naco.nic.in/vsnaco/indiascene/update).

# Nasolabial cyst with radiographic contrast medium: A case report

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## Abstract

Nasolabial cyst (NC) is a rare non-odontogenic soft tissue cyst occurring in sublabial area and anterior maxillary region. This cyst is frequently asymptomatic with the most usual sign being ala of the nose elevation. They are usually diagnosed in early stages because of cosmetic problems. Use of contrast medium is important for visualizing the definite extensions of NC primarily in cases when plain radiographs may not show any detectable changes. We report a case of Nasolabial cyst (NC) in a 35 year old female patient and discuss the diagnosis by contrast medium, differential diagnosis and treatment.

## Keywords

Nasolabial cyst, Images, Radiographic Contrast Medium, Fissural cyst.

## Introduction

Nasolabial cyst was first described in 1882 by Zukerkandi.<sup>1,5</sup> It is more common in adults, it has peak prevalence in the fourth and fifth decade of life. A greater incidence is seen in females (4:1).<sup>2</sup> It is usually unilateral in occurrence with no predilection for side.<sup>2</sup> However, 11.2% of cases have been reported to be bilateral.<sup>3</sup> Klestadt in 1913 suggested that NC arises from entrapped embryonic epithelium at the junction of the medial nasal, lateral nasal and maxillary processes, hence the termed as 'fissural cyst'.<sup>7,8</sup> The clinical presentation of NC is typical with an asymptomatic spherical swelling beneath the ala of nose causing its elevation and obliterating the nasolabial fold.<sup>9</sup> The lesion is usually asymptomatic unless it is secondarily infected. The teeth in the area of lesion are usually vital.<sup>4</sup>

## Case report

A 35-year-old female patient complained of swelling of 4 months duration on the upper right side of the face adjacent to the nose. The swelling started as a small and gradually increased to attain the present size. Patient was asymptomatic. Medical, Dental, Family and Personal histories were non-contributory. General physical examination revealed a normal gait, moderately built and nourished. All her vital signs were within normal limits. The face appeared asymmetric due to the swelling in the right ala of the nose region.

**On Extraoral Examination ;** A solitary ovoid shaped

swelling was present in the right nasolabial area of the face, measuring approx. 2 × 3 cms. Extending medio-laterally from the philtrum upto the right ala of the nose. The skin overlying the swelling did not show any secondary changes. The right nasal ala appeared elevated and left nasolabial fold was obliterated. On palpation the swelling was non-tender, soft in consistency, fluctuant and freely movable. (Fig.1)

**Fig.1:** Extraoral swelling in the right nasolabial fold



**Intraoral Soft tissue examination:** A solitary swelling in the region of upper right labial mucosa in the region of 11, 12 measuring approx. 2 × 2 cms superior-inferiorly, oval in shape. The swelling was non-tender, soft and fluctuant. Hard tissue examination revealed cervical abrasion seen in upper teeth. Vitality test revealed - 11, 12, 21, 22 were negative. On aspiration 2ml of cystic fluid was elicited. Swelling was asymptomatic, non tender, slow growing, present at anatomic location of the labial fold. 11, 12, 21, 22 were vital. On aspiration straw colored fluid was seen which suggest the possible Provisional Diagnosis of cystic lesion, could be a Fissural cyst. Differential Diagnosis of Nasoalveolar or Nasolabial cyst, Median palatal cyst, Nasopalatine duct cyst and Lateral periodontal cyst were included. (Fig.2)

Intra oral periapical radiographs i.r.t 11, 12 and Occlusal radiograph revealed no abnormality. 2ml of radiographic contrast medium (76% Urographin) was injected and Intra oral periapical, Occlusal and Panoramic radiographs were taken which revealed a radiopaque oval, kidney shaped lesions measuring 3cm in diameter.(Fig 3 and 4) .

**Treatment-** Enucleation of cyst was done under local anaesthesia (Fig.5)



**Fig.2:** Intraoral swelling in the right labial vestibule



**Fig.4:** O.P.G showing kidney shaped radiopacity i.r.t.11,12



**Fig.3 :** I .O.P.A radiograph in relation to 11,12 before and after injecting contrast media



**Fig. 5:** Enucleation of cyst under local anesthesia



patients with wide age distribution, but it is more frequent in the fourth and fifth decade, and occurs more in female than in males (ratio of male to female 1:6.5). Similar features were revealed in the present case. Clinical features of the NC are fluctuant swelling filling of the maxillary labial fold and the floor of the nasal vestibule, obliteration of the nasolabial fold and elevation of the alae of the nose. Similar features are in the present case. It sometimes does not show signs in routine intraoral radiographs. Aspiration of the cystic fluid and its replacement with radiographic contrast medium and then acquisition of radiographs, help with diagnosis and surgical planning of the Nasolabial cyst<sup>2</sup>.

Routine intraoral periapical radiographs are not diagnostic for Nasolabial cyst but assist in excluding other odontogenic or non-odontogenic cysts<sup>6,11</sup>. The visualization of Nasolabial cyst using radiographic contrast medium injection is a low cost, simple and rapid method. This procedure is precise for visualizing the definite extension of NC into the upper lip and nasal cavity, mainly in those cases where plain radiographs may not show any detectable changes and where CT can not be accessed<sup>2</sup>. In the present study the radiographic contrast medium was successfully used in evaluating the extent of nasolabial cysts.

The treatment can be made by surgical excision, via the sublabial incision, with very low recurrence rate and cosmetic reasons<sup>9,10</sup>. Same treatment procedure was carried out in the present case.

**Histopathology;** the section showed pseudostratified columnar epithelium and stratified squamous epithelium lining the cystic lumen with fibrous connective tissue and chronic inflammatory cells.

Based on the History, Clinical examination, Contrast radiography and Histopathology a final diagnosis of nasolabial cyst was confirmed.

### Discussion

The nasolabial cyst is a rare soft tissue cyst that occurs as a swelling in the nasolabial fold at the base of the alae of the nose.<sup>9</sup> Its frequency is around 0.7% of cysts of the jaws and 2.5% of the non-odontogenic cysts<sup>3,4</sup>. The NC affects



## Conclusion

Nasoalveolar cyst are benign cystic lesions that the radiologist may encounter incidentally or in conjunction with a mass immediately below the nasal aperture. Hence it should be considered in the differential diagnosis and can be diagnosed by routine radiographic technique with radiographic contrast medium.

## References

- 1 Valfrido Antonia PEREIRA FILHO et al. Nasolabial Cyst: Case Report, Braz Dent J 13 (3) 2002: 212-214
- 2 TMP Amaral, JB de Fatima da Conceicao, MCF de Aguiar, LM da Silva Fonseca and RA Mesquita: Nasolabial cyst with radiographic contrast medium: report of two casess :Dentomaxillofacial Radiology(2005),256-258.
- 3 Joel K. Cure, J.David Osguthorpe, and Pamela Van Tassel; MR of Nasolabial Cysts, AJNR:17, March 1996
- 4 Allard RHB, Nasolabial cyst. A review of the literature and report of case, Int J Oral Surg 1982; 11: 351-359.
- 5 Ahmet URAL, M. Hunturk ATILLA, Mesut TEZER, S.Sabri USLU; Bilateral Nasoalveolar Cyst: Case Report And Therapeutic approach.KBB-Forum 2007;6 (2).
- 6 Chinellato LEM, Damante JH. Contribution of radiographs to the diagnosis of nasoalveolar cyst. Oral Surg Oral Med Oral Path 1984; 58; 729-735.
- 7 A Textbook of Oral Pathology; Shafer, 5th edt.Shafer-Hine-Levy.
- 8 Jin Ho Choi, Jae Hoon Cho, Hee Joon Kang et al; Nasolabial cyst: a retrospective analysis of 18 cases-Original Article- Brief Article; Ear Nose Throat Journal, Feb,2002.
- 9 Caner Sahin, Case Report Nasolabial cyst; Case Report in Medicine; Volume 2009.
- 10 Jae Yong Lee, Byoung Joon Baek, Jang Yul Byun, Hyuck Soon Chang, Byung Don Lee, Dong Wook Kim; Comparison of Conventional Excision via a Sublabial Approach and Transnasal Marsupialization for the Treatment of Nasolabial Cysts: A Prospective Randomized Study; Clinical and Experimental Otorhinolaryngology Vol. 2, No.2: 85-89, June 2009.
- 11 Van Bruggen AP , Shear M, Du Preez IJ, Van Wyk DP, Beyer D, Leeferink GA. Nasolabial cyst: a report of 10 cases and a review of the literature. J Dent Assoc S Afr 1995; 40: 15-19.

# Drug induced Erythema Multiforme: A case report

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## Abstract

Erythema Multiforme is a rare, acute, inflammatory mucocutaneous condition caused by a hypersensitivity reaction with the appearance of cytotoxic T lymphocytes in the epithelium that induce apoptosis in keratinocytes, which leads to satellite cell necrosis. Reactions to drugs are quite common and are generally mild, hence not reported. However, occasionally life threatening reactions including Erythema multiforme major (Steven Johnson's syndrome) and Toxic Epidermal Necrolysis may occur. A wide spectrum of drugs can sometimes give rise to Erythema Multiforme. We report a case of Erythema Multiforme in a 4 year old female following administration of Non Steroidal Anti-Inflammatory Drugs.

## Keywords

Erythema Multiforme, Drug Reaction, Hypersensitivity Reaction.

## Introduction

Erythema Multiforme (EM) is an acute inflammatory disease that affects skin and/or mucous membranes that cause a variety of skin lesions, hence the name-multiforme. EM usually affects apparently healthy young individuals with the peak age of 20-40 years although 20% of cases are young children.<sup>1</sup>

It has been classified into several variants, mainly minor, major and severe forms, as it may involve the mouth alone, or may present with a skin eruption, with or without lesions of other mucous membranes. EM typically affects only one mucosa, and may be associated with symmetrical target skin lesions on the extremities. EM major typically involves two or more mucous membranes with more variable skin involvement termed Stevens- Johnson syndrome.<sup>2</sup> A severe variant of the disease is TEN (Toxic Epidermal Necrolysis, Lyell's disease), which results in sloughing of skin and mucosa in large sheets. Morbidity is high and patients with this form of disease are managed in burn centers where necrotic skin is removed under general anesthesia.<sup>3</sup>

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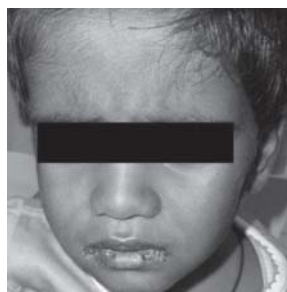
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**Drug related Erythema Multiforme-** A wide range of drugs- especially NSAIDs, barbiturates, cephalosporins, phenothiazines, progesterones, protease inhibitors, sulphonamides, sulphonylurea derivatives and tetracyclines- may give rise to Erythema Multiforme, and it may be clinically impossible to distinguish drug induced erythema multiforme from disease due to other causes<sup>4</sup>

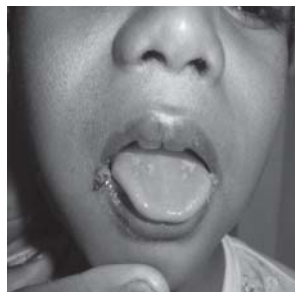
## Case report

A 4 year old female child reported to the department of Oral Medicine and Radiology, with the chief complaint of painful ulcers on the tongue, lips and palate since 2 days due to which she was unable to open her mouth and eat anything. Her mother informed that when she tried to clean the patient's mouth with her finger, uncontrolled, fresh bleeding occurred. Medical history revealed that patient took medication for fever and throat pain from a physician 4 days back. On the second day after taking that medicine, she developed ulcers on the lips and in the mouth along with fever. No previous history of uncontrolled bleeding was reported. Personal history and family history were non contributory. On General Physical Examination, all Vital Signs were normal except temperature which was 99.5°F. Extraoral examination of the lesion revealed diffuse erythematous areas on the vermilion borders of lips, covered by pseudomembranous slough and crustations on the left corner of the mouth. Bleeding areas were present on corners of the mouth Intra-oral examination was compromised at the first visit, as the patient was unable to open her mouth. When patient reported after 3 days of our treatment, she was able to open her mouth and diffuse areas of ulcerations were seen on the tongue (Fig 1 and Fig 2).

**Fig 1:** Crustations on lips



**Fig 2:** Ulcerations on tongue

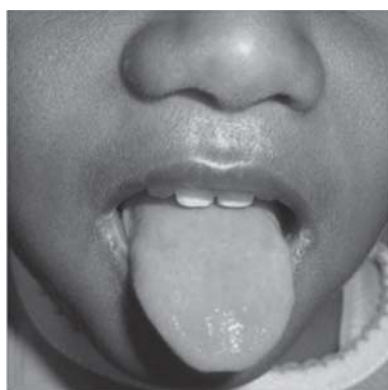


On the basis of history and clinical examination, a diagnosis of Drug induced Erythema Multiforme. Management was done by giving 15 mg of prednisolone once daily for 3 days and subsequently the dose was reduced to 10 mg for the next 3 days, the 5 mg for next 3 days. After 10 days of medication, intra as well as extra-oral bleeding had stopped and the lesions were completely healed (Fig 3 and Fig 4)

**Fig 3:** Post treatment (Crustations healed)



**Fig 4:** Post treatment (Ulcers healed)



Symptomatic relief was given by Topical anesthetic mouthrinse (benzadamine hydrochloride) twice a day. A complete hemogram was advised which reported absolutely normal counts of the blood cells. Hence, the differential diagnosis of "Drug Induced Thrombocytopenic Purpura" was ruled out.

## Discussion

Erythema multiforme (EM) is a typically mild and recurring mucocutaneous reaction characterized by target or iris lesions of the skin or mucous membranes which resolve within 1 to 6 weeks.<sup>5</sup> The best documented trigger factor for EM is drugs (as reported by our patient) and microorganisms in 80-90% of cases. The drugs frequently associated with EM are sulfonamides, nonsteroidal anti-inflammatory agents, penicillins, trimethoprim, barbiturates and carbamazepine. The documented microorganisms responsible are *Mycoplasma pneumoniae*<sup>6</sup> and herpes simplex- 1 and 2 viruses in 70-80% of cases. HSV antigens are however, expressed on the endothelial cells of the blood vessels. The fragments of HSV DNA are detected in lesions by in situ hybridization and by polymerase chain reaction.<sup>7</sup>

Other triggers for EM include benign and malignant tumors, radiotherapy, Crohn's disease, sarcoidosis, histoplasmosis and infectious mononucleosis. The pathology of EM is that there is a perivascular infiltrate of CD4 and CD8 lymphocytes surrounding swollen blood vessels in the upper dermis with papillary dermal edema and vacuolar degeneration of the basal layer, subdermal blister formation and epidermal necrosis of keratinocytes that increases with older lesions. The individual necrotic keratinocytes are surrounded by CD8 cells, termed "satellite cell necrosis".<sup>8</sup>

**Clinical Presentation:** Oral mucosal lesions occur in more than 70 % of cases of EM. Preferred sites of involvement include the lips, alveolar mucosa, and palate. Lip involvement is almost universal (as seen in the case reported). Although target or iris lesions may be seen, superficial ulcerations or crusted lesions are more common. An episode of recurrent HSV may precede the lesions of EM; the average interval between the onset of an episode of recurrent HSV and EM is 8 days (range, 2-17 days).<sup>9</sup> Despite this interval, it may be difficult to distinguish the initial herpes labialis lesion and lip lesions of EM.<sup>10</sup>

**Diagnostic Techniques:** The diagnosis of EM is based on history and the clinical presentation. Laboratory investigations typically reveal no abnormalities of significance.<sup>9</sup>

**Management:** Mild cases of EM may be treated with supportive measures only, including topical anesthetic mouthwashes. Moderate to severe oral EM may be treated with a short course of systemic corticosteroids in patients without significant contraindications to their use. An initial dose of 30 mg/day to 50 mg/day prednisolone or methylprednisolone in tapering dose is considered helpful in shortening the healing time. Higher doses of steroids are considered necessary for severe cases. Prophylactically, Acyclovir can be used to prevent HSV-related EM.<sup>3</sup>

## Conclusion

Nonsteroidal anti-inflammatory drugs (NSAID) are widely

used and Erythema Multiforme is its rare adverse effect. The diagnosis of EM is solely based on history and clinical examination. Treatment focuses on prevention of HSV infection, identifying the drug responsible and indefinite avoidance of the culprit drug. This article is therefore, to make the general practitioner aware of the side effects of commonly prescribed NSAIDs.

## References

1. Crispian Scully, Jose Bagan. Oral mucosal diseases: Erythema multiforme. *British Journal of Oral and Maxillofacial Surgery* 2008; 46: 90-95.
2. SR Isik, G Karakaya, G Erkin, AF Kalyoncu. Multidrug-Induced Erythema Multiforme. *J Investig Allergol Clin Immunol* 2007; Vol. 17(3): 196-198.
3. Martin S. Greenberg. Ulcerative, Vesicular, and Bullous Lesions. *Burkett's Oral Medicine*, Ninth edition 1994; Chapter 2 (pp 20-22): J.B. Lippincott Company, Philadelphia.
4. C. Scully, J.V. Bagan. Adverse Drug Reactions in the Oro-facial Region. *Crit. Rev Oral Biol med.* 2004; 15(4): 221-239.
5. P Sen, SH Chua. A Case of Recurrent Erythema Multiforme and its Therapeutic Complications. *Ann Acad Med Singapore* 2004;33:793-6.
6. C Leaute-Labreze, T Lamireau, D Chawki, J Maleville, A Taieb. Diagnosis, classification, and management of erythema multiforme and Stevens-Johnson syndrome. *Arch Dis Child* 2000; 83: 347-352.
7. LY Chan, WYM Tang, CY Leung, KK Lo, Recurrent erythema multiforme in a child. *HKMJ* September 2000; Vol. 6: No 3
8. P. Michele Williams, Robert J. Conklin. Erythema Multiforme: a review and contrast from Stevens-Johnson syndrome/toxic epidermal necrolysis. *Dent Clin N Am* 49 (2005) 67-76.
9. Neivell, Damm, Allen, Bouquot. *Oral and Maxillofacial Pathology*, Second Ed. 2008; Chapter 16: Page no. 674-676. Saunders, An Imprint of Elsevier.
10. Jordi Castellsague, Luís-Alberto García-Rodríguez, Alberto Duque and Susana Pérez. Risk of serious skin disorders among users of oral antifungals: a population-based study. *BMC Dermatology* 2002, 2:14.

# Cross sectional survey of burden of illness in terminally ill cancer patients

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## Abstract

## Introduction

Cancer is one of the leading causes of mortality in women, especially in the developing countries, where palliative care is not greatly emphasized.

## Objectives

The primary objective is to analyse the various medical, ethical and legal issues faced by terminally ill gynaecological cancer patients.

The other objectives being pain assessment, overall health related quality of life, economic issues and to determine preferences regarding decision making and information disclosure to patients.

## Methods

A non interventional hospital based cross-sectional survey of 100 terminally ill patients was conducted over a period of 2 years (March 2007 – April 2009). With an informed consent, the patient is asked to complete a questionnaire.

## Results :Medical problems

74% of patients had intolerable pain, so deprived of sound sleep. 98% of them suffered from some form of depression. Poor educational status and poverty made these patients highly dependable on family members for financial assistance (64%). Comparatively the more elderly patients experienced an inner fear, as they were neglected or abandoned by the care takers.

## Ethical problems

With good doctor-patient relationship, communication about diagnosis and management was established in 50% of cases, but majority of them (81%) were not involved in decision making, which amounts to medical negligence.

## Legal problems

None of the patients were aware of their legal rights during the course of their illness

## Introduction

## Background and rationale

Cancer is a global health problem, several million cases are being diagnosed each year. The developing countries are facing greater problems handling end stage cancer patients. In India about 1,00,0000 new cases of cancer are detected out of which 80% are already in advanced stage.<sup>1</sup> Terminally ill means, having an incurable or irreversible condition that has a high probability of causing death within a relatively short time, with or without treatment, probably by one year.

Most cancer patients end up with a terminally ill state, where the management of these patients moves from disease control to improving quality of life. This can be achieved by palliative care.

## Medical problems faced by terminally ill patients

Terminally ill cancer patients encounter various medical problems, which could be physical symptoms like asthenia, dysnea, cachexia, nausea, vomiting, edema, skin sores etc., psychiatric symptoms like confusion, depression delirium are troublesome. Social and economic burden on the family members, dependence on others, further detourates the health of the patient. Pain burden tender to become chronic in nature.

## Principles of palliative care

A dedicated palliative care team forms an integral basis towards good palliative care.

## WHO (2002) defines palliative care as

An approach that improves the quality of life of patients and their families facing the problems associated with life-threatening illness, through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other problems, physical, psychosocial and spiritual.<sup>2</sup>

## Key points from this definition

- Quality of life
- 4 domains – physical, social, emotional, spiritual / existential
- QOL changes
- Unit of care
- Patients and family
- Patient-centered care and communication

- Holistic care
  - Physical, psychosocial, spiritual
  - Active management
- Continuum of care

Palliative care is all about good and honest communication with the patient about the illness, its implications, expected care, involvement of the family members, setting realistic goals regarding good symptom management and improve the quality of life.

Psychological support is of prime importance, which goes unnoticed (60%) psychological distress impairs patient's capacity for acceptance and amplifies pain and depression. Moral support can enhance self esteem and coping ability. A good communication, maintaining hope, setting realistic goals and improving quality of life is the duty of the treating doctor.

Patients should be able to face death, overcome the threat of dying and death may be experienced without coercion. In India, plight of women suffering from terminal cancer is even worse, due to gender differentiation, a woman is physically and socially isolated and sometimes rejected by the family.

The WHO estimates that 4 billion people (80% of the world) use herbal medicine for some aspect of primary health care.<sup>3</sup>

Non availability of opioids lead to poor pain control, as there are restrictive laws over the manufacture, distribution, prescription and dispensing of opioids. Pain could be physical, psychological, social or spiritual, needs to be dealt in a multifaceted manner.

### Ethical issues in palliative care

A high standard of palliative care requires ethical sensitivity, an understanding of the legal dimensions of the clinical situation and good compassion skills.

Patients autonomy should be respected, by providing information and ensuring that the patient gives consent before any medical intervention.

### Ethical issues in palliative care<sup>4</sup>

#### Based on four principles

##### a) Respect for patient autonomy

- Recognizing a person's right and capacity to think, decide and act for herself according to her beliefs, values and a life plan.
- Truth telling is fundamental to the integrity of both parties in the patient-doctor relationship.

##### b) Justice

- Balancing needs of individuals with that of society.
- Distributive justice – same care for patients in similar situations.
- Terminally ill patients are not always seen as worthy of our financial resources, time, hospital facilities or professional efforts.

##### c) Beneficence

- Implies positive acts and clinical strategies to reduce suffering and increase well-being.

##### d) Non-maleficence

- Causing unnecessary physical pain or psychological pain or suffering during physical examinations, tests or procedures.

Compassion is an essential component of the doctor-patient relationship.

Ethically, patients have the right to effective pain relief and palliative care that respects their individuality. Personally patients need and deserve love, respect and spiritual support.

The human rights of the moribund include liberty, dignity, personal integrity, information, assistance and relief from unnecessary suffering. Implicit in these rights is the right to choose the home as the place to die. Dying at home allows loving care, mutual gratification, reconciliation, reflection and reciprocity before departure.

### Legal problems of palliative care

The fear of diversion of morphine for non medical uses has led to severe control on its availability. The courts have issued directions to improve the availability of the drug, yet 97% of Indian patients have very poor access to the drug.

By Indian constitutional law, Article-21 does not include the right to die, Sec.309 IPC deals with attempt to suicide and Sec.30 deals with abatement.

However as far as qualitative life in terminally ill cancer patients are concerned, euthanasia comes into question.

- Euthanasia – Greek origin – ‘a good death, a gentle, easy death’ It goes against the Hippocratic oath.

Active Euthanasia : Taking deliberate action to end a patient's life

Passive Euthanasia : Withdrawing treatment with the aim of ending life

Assisted suicide : Providing the means to allow a patient to end their own life. It is illegal in India.<sup>5</sup>

Physician assisted suicide (PAS) is done in the “best interests” of the patient, though it is illegal in our country. Some countries like Holland, Dutch, Colombia, Japan, Oregon do allow PAS in certain circumstances.

Moral, ethical and religious issues pertaining to euthanasia embrace subjects as diverse as “patient autonomy”, “quality of life”, “sanctity of life”, “death with dignity”, “patients rights” The terminally ill law, UK, 2006-2007 deals with the manner of treating terminally ill patients, balancing with autonomic will of patients, value of the sanctity of life and society, quality of life and actual existence. It upholds the concept that the right to die with dignity is part of the right to live with dignity.<sup>6</sup>

Law relating to use of experimental drugs, the Washington legal foundation (WLF) 2007 urged the U.S. court of appeals to grant terminally ill patients a constitutionally based right to access to experimental drugs, not fully approved by FDA.

WLF is a public interest law.<sup>7</sup>

Legally patients have a right to choose or refuse treatment with full knowledge of the benefits and risks. Informed consent, relevant information disclosure, and proper documentation of the course of management is another legal requirement :

#### **Terminal sedation**

- The treatment proposed must be beneficial or at least neutral.
- The good result (e.g., relief of suffering) must outweigh the untoward outcome (e.g., hastening death)

#### **Right to dignity**<sup>8</sup>

- Access to good symptom control
- A choice over place of death and
- Holistic care.

#### **Effective communication**

Honest two-way communication with health professionals is of prime importance.<sup>9</sup>

Patients have the right to make their own decisions through spoken words or living will. In unconscious patients, their family has the right to make decisions for them.

#### **Dying with dignity**

- Requires decision to down regulate intensive life prolonging care and up regulate palliative care, is considered after discussing with care takers.

Legal provisions

like Living wills, advance directives

(eg., DNR), assignments of power of attorney, are some issues which the end stage women can avail.

### **II) Study objective**

#### **Primary objective**

To analyse the various medical, ethical and legal issues faced by terminally ill cancer patients.

#### **Secondary objectives**

1) Pain Assessment :

- Duration and severity of pain
- Treatment patterns
- Patient satisfaction with treatment

2) Overall health related quality of life impairment

- Co-morbidities (especially sleep disturbances, anxiety, depression)
- Quality of life

3) Economic burden

- Financial burden

4) Determine preferences regarding decision making and information disclosure to patients.

### **III). Study design and study population :**

**Type of study:** A non interventional, hospital based, Cross sectional survey was done.

**Place of study :** S.S. Institute of medical sciences, Davangere, Dept. of Surgical Oncology.

**Duration of study:** 2 years (March 2007 – April 2009)  
Institutional ethical committee clearance taken for the study.

### **IV). Subject eligibility criteria**

**1) Sample size :** 100 palliative care patients

#### **2)Inclusion criteria :**

- Diagnosed terminally ill gynaecological cancer patients
- Adult women included
- Inpatient and outpatient department patients included
- Willing to participate.
- Should be able to understand and comprehend

#### **3) Exclusion criteria :**

- Children below 18 yrs excluded
- Non gyanecological cancer patients were excluded

### **V). Study procedure**

The investigator will inform the patient about the study, informed consent is taken, then patient is asked to complete a questionnaire, by him/herself or the physician can ask the questions himself and note the answers.

### **Methodology**

The patient was asked to complete the questionnaire herself or the investigator will ask the questions and note the answer.

Pain assessment – Universal pain assessment tool.

### **Parameters to asses medical problems were :**

- Physical : Pain, dysnea, bleeding, foulsmelling discharge, asthenia, cachexia, nausea, vomiting, edema, sores, insomnia.
- Psychiatric / Psychological problems : Confusion, irritability, depression, delirium.
- Social and economic burden
- Emotional support

### **Ethical problems assessed were :**

- Good doctor patient relationship
- Effective Communication
- Good symptom control
- Withholding treatment
- Religious concerns
- Decision making
- Place and mode of death

### **Legal problems taken into consideration were:**

- Informed consent

- Documentation
- Euthanasia
- Terminal sedation
- Living wills
- Participation in clinical trials
- Abandoned from home
- Legal rights

**Results**

**Age group : 30-82 years**

**Socioeconomic status : Middle to lower**

**Literacy rates : Low**

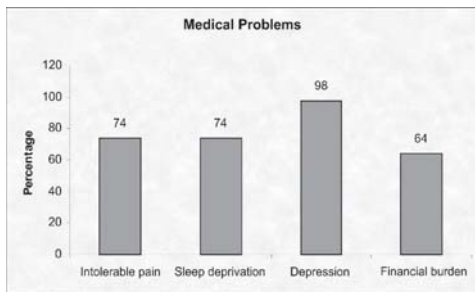
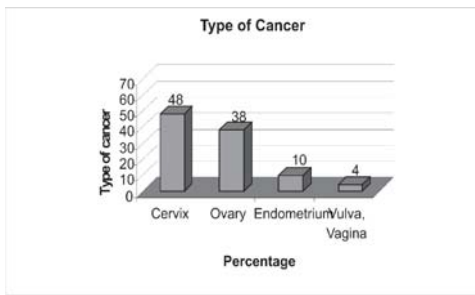
**Type of cancer**

Almost 98% of women suffered from depression and intolerable pain with sleep deprivation was seen in 74% of women and 64% had some financial burden to access medical care.

**Ethical problems**

Majority of these patients (81%) had a good doctor patient relationship, but this lacked a honest two way

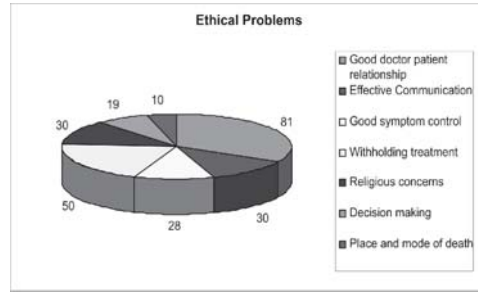
**Fig. 1:**



communication (30%) leading on to noninvolvement in decision making (19%). Only 28% had good symptom control, while the relatives of 50% of these patients requested to withhold further treatment as its just a palliative approach. 30% did have some religious concerns. As the truth of their end stage disease was not revealed to them and so only 10% had made up their mind regarding the place and mode of death which definitely was their home and a peaceful death was their choice.

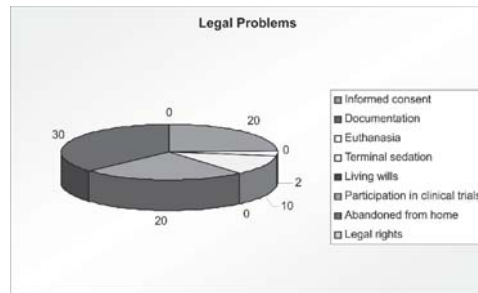
**Legal problems**

**Fig. 2:**



Many of the legal issues were not considered during the care of these palliative care patients. Informed consent was taken from 20% of women. Documentation of the event was very poor probably due to lack of assistants to monitor progress. None of the patients knew about their legal rights nor made any living wills, 2% requested for euthanasia which was deferred, 10% received terminal sedation in the form of morphine patches, 20% did opt for participating

**Fig. 3:**



in clinical trials in a hope of being useful to mankind and it is sad to know that 30% of these women were abandoned from home and stayed at the hospital for long periods.

**Discussion**

**Palliative care in the developing world**

Limited resources (and late presentation) mean that disease-oriented care is not available to many patients at the time of diagnosis.

**Management of the dying patient :**

- Explanation to patient and family
- Symptom management
- Rationalise medication and discontinue non-essential needs
- Continue/institute medication for symptom control.
- Route of administration (syringe driver)
- Psychosocial support
- Spiritual support.

**Does it end here ?**

- No !!!!!
- End of life care doesn't mean NOT doing anything and just letting the patient die



- It is NOT about “giving up”
- Withdrawal of life prolonging treatments doesn't mean NO treatment.
- It is active total care to provide the best quality of life until death.

## Conclusion

Cancer patients in India are a neglected lot, more so the women are left to suffer, less than 1 % of them have access to palliative care.

- We need to create interdisciplinary awareness of end of life care.
- Develop good communication skills and provide emotional support by dedicated palliative care team
- Involvement of government and legislative bodies to enforce suitable laws regarding care of terminally ill cancer patients.
- Less stringent legislation for the appropriate use of opiates in pain management.
- Ethical issues and rights of patients to be considered at every step of management
- Principles of palliative care should be taught to every doctor as an undergraduate.
- Media should be involved to public awareness about palliative care. More palliative care centres are needed

to provide medical care for terminally ill cancer patients.

## References

1. Dr. Partha Basu “Palliative care an integral part of cancer management”, Vol. VI, I, Indian Journal of Oncology, Page 5-13, (2006)
2. Sepulveda et al., JPSM 2002,24:91-96.
3. Reena George, “Evaluation of palliative care in developing countries”, Vol. II, I, Indian Journal of Palliative care, page 2-6 (2005).
4. Ethical and legal issues surrounding palliative care, International conference on modern cancer management, July 2008;21-27.
5. Euthanasia and physician assisted suicide, 2002, pg. 2-10, www.spuc.org.uk.
6. www.worldtd.net/public/Israel\_terminallyill\_law.pdf
7. Euthanasic and physician assisted suicide, 2002,pg 2-10, www.spuc.org.uk.
8. Pincombe et al (1997)
9. Ethical and legal issues – International conference on modern cancer management, July 21-27, 2008.
10. Current review of pain, Gerald et al. eds. Prithvi Raj, 2000.
11. Christine faull et al., Handbook of palliative care, 2001.

# Prevalence of HIV in patients attending Integrated counselling and testing centre – RIMS General Hospital, Kadapa

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## Abstract

AIDS is a new disease, which came to light only in the year 1981 when it caused out

Breaks in the USA. The origin of the virus has been the subject of much controversy, reminiscent of the situation 500 years ago, syphilis was first recognized. It has been suggested that the virus may have originated in Africa, perhaps from a simian. Immunodeficiency and spread to the USA probably through Haiti. In the permissive American Society of the 1970's the virus spread widely among male homosexuals and drug addicts, finally to come out into the open as outbreaks in 1981. HIV infection was detected rather late in India. The first cases having been found in female sex workers in Madras in 1986.

## Keywords

ICTC Centre, No of clients tested for HIV, No of clients receiving HIV tests results, Total No of clients testing Sero – Positive.

## Introduction

### Morphology

HIV is spherical enveloped virus about 90 – 120 nm in size. The nucleocapsid has an outer icosahedral shell and in inner cone shaped core enclosing the ribonucleoproteins. The genome is diploid composed of two identical single stranded positive sense RNA copies.

In association with viral RNA is the reverse transcriptase enzyme which is a characteristic feature of retroviruses. When the virus infects a cell the viral RNA is transcribed by the enzyme, first into single strand DNA and then double strand DNA (Provirus) which is integrated into the host cell chromosome. The provirus can remain latent for long periods, though it influences host cell functions. At times in response to viral promoters the provirus initiates viral replication by directing synthesis of viral RNA and other components. During viral replication when the naked virus buds out through the host cell surface membrane it acquires a lipoprotein envelop, which consists of lipid derived from the host cell membrane and glycoproteins which are virus coded. The major virus coded envelop proteins are projecting knob like spikes on the surface and the component of the virus, which binds to

the CD4 receptors on the susceptible host cells.

## Immunology

Viral Genes and Antigens: the genome of HIV contains three structural genes (gag, pol and env) characteristic of all retroviruses as well as other non structural and regulator genes specific for the virus. The product of these genes both structural and non – structural acts as antigens. Sera of infected person contain antibodies to them. Detection of these antigens and antibodies is of great value for the diagnosis and prognosis of HIV infection.

Antigenic Variation and Diversity of HIV: HIV is a highly mutable virus. It exhibits frequent antigenic variation as well as differences in other features such as nucleotide sequences cell tropism growth characteristics and cyto pathology.

Antigenic variation is most frequent in respect of the envelop proteins but is also same less often with other antigens. Based on the antigenic differences two types of HIV has been recognized. The original isolates of HIV and the related strains prevalent all over the world belong to HIV Type – 1. HIV strains react with HIV Type – 1 anti serum very weakly are not at all have been termed HIV Type – 2. The envelop antigens of the two types are different through these core polypeptides show some cross reactivity. HIV – 2 has only 40% genetic identity with HIV-1. It is more closely related to simian immunodeficiency virus than to HIV-1. HIV-1 strains have been classified into 9 sub types based on sequence analysis of these gag and env genes. These sub types are designated as A – I.

## Transmission and pathogenesis

### Transmission

HIV is primarily a sexually transmitted infection in the USA. It has transmitted predominantly among male homosexuals. The danger of infection is more for the passive partners because mucosal tears are very frequent during anal intercourse and virus leading to lymphocytes in the semen can directly enter through these.

The second mode of transmission is through transmission of blood and Blood products. Before the danger of HIV transmission was recognized many persons had received blood and blood products containing the infectious virus.

**Table 1:** from April – 2009 to March – 2010

S. No.	Months	Counselled and Tested				Reactives				Voluntary Counseling and Tested				Reactives			
		M	F TG	TS /	total	M	F TG	TS /	total	M	F TG	TS /	total	M	F TG	TS /	total
1	APRIL – 09	374	246	0	620	50	36	0	86	258	164	0	422	39	27	0	66
2	MAY-09	319	167	0	486	56	30	0	86	240	102	0	342	39	22	0	61
3	JUNE-09	489	314	0	803	68	46	0	114	313	198	0	511	50	33	0	83
4	JULY-09	365	404	337	1113	43	46	36	125	273	245	0	518	37	29	0	66
5	AUGUST-09	498	436	0	934	47	40	0	87	172	64	0	236	19	14	0	33
6	SEPTEMBER-09	420	288	0	709	38	23	1	61	148	93	0	201	16	09	0	25
7	OCTOBER – 09	560	317	0	877	16	44	0	104	166	94	0	260	21	08	0	29
8	NOVEMBER – 09	539	302	0	841	64	25	0	89	173	139	0	366	22	09	0	31
9	DECEMBER-09	377	249	0	626	47	19	0	66	91	61	0	152	16	13	0	29
10	JANUARY-10	433	265	0	698	53	24	0	77	76	43	0	119	26	11	0	37
11	FEBRUARY-10	339	217	0	616	43	19	0	62	129	61	0	190	18	11	0	29
12	MARCH-10	513	480	4	997	62	34	2	98	145	118	4	267	18	14	02	34
	Total	5286	3685	314	8971	631	386	39	1056	2184	1382	4	3570	321	200	02	523

M = Male, F = Female, TS= Trans Sex, TG = Trans Gender.

Contaminated Needles can transmit the infection. Needles used to inject drugs can transmit HIV when they are used by more than one person. Needle should never be shared but if they are shared they should be thoroughly between uses.

HIV can be transmitted from mother to fetus/baby while it is still in the uterus during the delivery process and through breast feeding. There is strong evidence that use of anti-viral medications during pregnancy can reduce maternal transmission of HIV.

### Pathogenesis

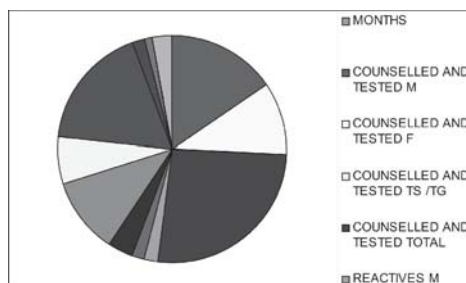
The receptor for the virus is the CD4 antigens and therefore the virus may infect any cell bearing the CD4 antigen on the surface and so are susceptible to infection. Infection is transmitted when the virus enters the blood or tissues of a person and comes into contact with a suitable host cell principally the T4 lymphocyte. Infection is likely to result more often following the introduction of HIV infected cells than of cell free virus. The double strand DNA transcript of viral DNA is integrated the genome of the suspected cell causing a latent infection. From time to time lytic infection is initiated releasing progeny virions which infect other cells. The long and variable individual HIV can be isolated from the blood lymphocytes cell free plasma, semen, cervical secretion, saliva, tears, urine and breast milk. The primary pathogenic mechanism in HIV infection is the damage caused to T4 Lymphocytes. The T4 cells decreases in No. and the T4: T8 cell ratio is reverse. Viral infection can suppress the function of infected cells without causing structural damage. Infected T4 cells don't appear to release normal amounts of interleukin-2 and Gamma interferon and other lymphokines. This has a mark

dampening effect on cell mediated immune response.

### Case history

Prevalence of HIV in patients attending Integrated Counseling and Testing Centre in RIMS General Hospital for the academic year of April-2009 to March-2010.

**Table 1:** graphically



### Discussion

Health education, Sex Education and Awareness programs are important to prevent the Retro Viral Positive cases in society.

### References

1. Ananthanarayana and Paniker's Text book of Microbiology – seventh edition.
2. Pathology third edition (Emanuel Rubin, John L.farber).
3. Davidson's principles and practices of medicine – eighteenth edition.

# Utility of paper pencil tests for the assessment of psychomotor performance-a study with chlorpheniramine

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## Abstract

## Background

The effects of drugs on psychomotor performance have been investigated using a variety of techniques. But the various techniques used are often complex and sometimes inconvenient. Paper and pencil tests do not need complex equipment, they are easy to administer and replicate. That's why the present study was planned to assess the utility of paper pencil test for conducting psychomotor studies.

## Materials and methods

Following each single dose of chlorpheniramine 4 mg or placebo, 24 subjects performed paper pencil tests- six digit cancellation test, digit symbol substitution test and arithmetic ability at 0, 2, and 4 hours interval. Subjective assessment was done by three different visual analogue scales in the double blind placebo controlled study.

## Results

In all the paper pencil tests performance was impaired by chlorpheniramine significantly at 2 hours and 4 hours in comparison to placebo. These findings were also reflected in the subjective assessment of visual analogue scales.

## Conclusion

It can be concluded from the study that paper and pencil tests are useful tools for the assessment of psychomotor performance. Paper pencil test should be the part of battery of psychometric tests.

## Keywords

Paper pencil test, Six digit cancellation test, Digit symbol substitution test, Arithmetic ability, Visual analogue scale.

## Introduction

Our brain is complex structure with diverse variety of functions. Any drug which crosses the blood-brain barrier

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can stimulate or depress the central nervous system. Amongst various effects produced by the drugs, sedation is one of the important effects. A drug which induces sedation impairs cognitive and psychomotor functions. Notably, day time sedation (psychomotor impairment) disturbs the ability to perform daily work such as driving a vehicle and operating machinery, and thus increases the risk of accidents.<sup>1</sup>

Psychomotor performance involves numerous sub-functions, and cannot be treated as a unit.<sup>2</sup>The correct approach to the study of drugs on psychomotor performance is to break down complex skill into their components<sup>3</sup>. Psychomotor performance results from the co-ordination of sensory and motor system through the integrative and organizational process of brain and central nervous system.<sup>4</sup> Complex feedback and adaptive systems complete the process by which environmental stimuli produce appropriate, coordinated behavioural responses. The effects of drugs on psychomotor performance have been investigated using a variety of techniques. But the various techniques used to assess the psychomotor functions are diverse often complex, frequently insensitive to drug induced changes and sometimes inconvenient to enact or replicate. In this context pencil and paper tests are attractive because they do not need complex equipment, they are easy to administer and replicate<sup>5</sup>. That's why the present study was planned to assess the utility of various paper pencil test for conducting psychomotor studies. In the present study chlorpheniramine was compared with placebo because it is a classical (1<sup>st</sup> generation) H<sub>1</sub>-antihistamine<sup>6</sup> which has side effects like impairment of psychomotor performance<sup>7, 8</sup>.

## Materials and methods

Before beginning the study ethical approval was obtained from the institutional ethics committee. It was a double blind, cross-over study in which sample size of twenty four was calculated at the level of significance  $\alpha = 5\%$  and power 80% by the institutional statistician. Subjects receiving other drugs (e.g. sedatives, antianxiety, antihistamines), history of allergy, hypersensitivity to any medications and smokers and alcoholics were excluded from the study. 24 healthy volunteers of age group between 18 to 20 years were included in the study after taking written informed consent.

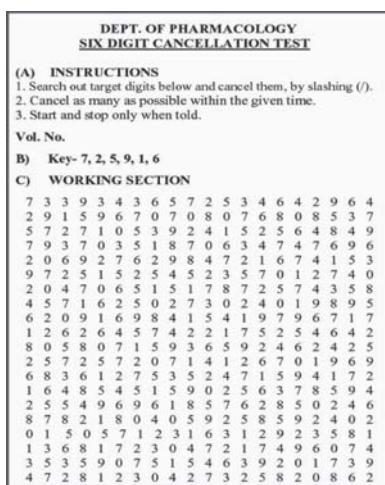
Instructions were given to the volunteers 2 days prior the

day on which the study was to be carried out. The volunteers were asked to refrain from smoking<sup>9</sup>, drinking alcohol or taking any medication. Before beginning the study, the subjects were explained about the experimental procedures and the psychomotor function tests. The volunteers received training till a performance plateau was reached with the battery of psychomotor tests in order to preclude any learning curve effect. On the day of study, drinking tea or coffee was prohibited<sup>10,11</sup>. Instructions were given to the volunteers not to eat anything on the study day except drinking water after the breakfast till the study was completed. They would perform their routine tasks except those involving mechanical work or driving vehicle which was strictly avoided. Each of the volunteer acted as his own control and each volunteer got each formulation by making cross over with a washout period of one week between any two of the drugs. Following each single dose of chlorpheniramine 4 mg or placebo, subjects performed a series of psychomotor performance tests at 0 hours, 2 hours and 4 hours post dose. Various objective paper pencil tests performed by the subjects were six digit cancellation test<sup>4</sup>, digit symbol substitution test<sup>4</sup>, arithmetic ability<sup>5</sup> and subjective tests such as three different visual analogue scales<sup>12</sup>. On the study evening, the subjects were instructed not to drive a vehicle.

### Six digit cancellation test (SDCT)

Volunteers were given a sheet consisting of 1200 randomised digits arranged in 40 columns (Photograph-1). During two minutes time period the subject had to cancel as many target digits as possible and mark the point up to which the cancellations attempted. The six key digits in the working section were changed randomly so as to avoid the effect of memory or practice during repeated administration of the test. Scoring was given on the basis of number of correct cancellations.

Photograph-1

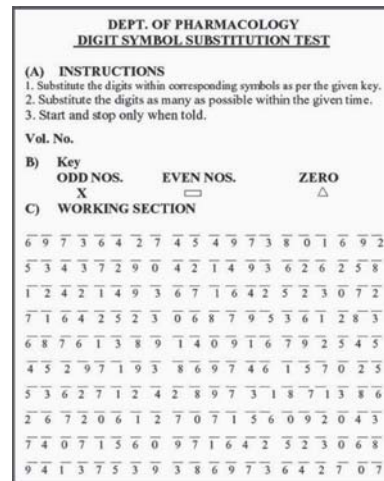


### Digit symbol substitution test (DSST)

In DSST the subjects were required to insert a symbol

above each digit during two minutes time period for odd, even and zero numbers on a given sheet of 200 randomized digits arranged in 10 rows and 20 columns (Photograph-2). Parallel worksheets were prepared by changing the symbol for the digits in the working section so as to avoid the effect of memory during repeated administration of the test. Scoring was done on the basis of number of correct substitutions.

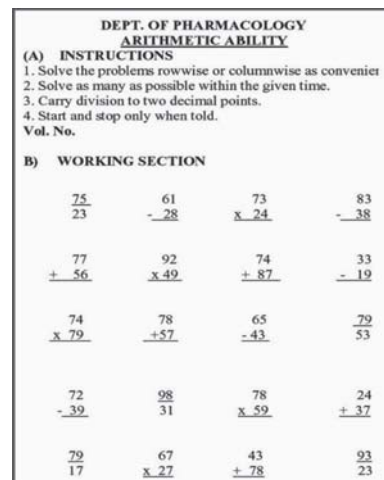
Photograph-2



### Arithmetic ability test (A.A.)

The worksheet contained simple mathematical problems i.e. addition, subtraction, multiplication and division (Photograph-3). Division had to be carried to two decimal points. The problems were randomly distributed through the sheet in 5 rows and 4 columns and volunteers were asked to solve the problems during the two minutes time period. The score was given depending upon the number of correct problems solved.

Photograph-3



### Visual analogue scales

For subjective component, three different visual analogue

## Photograph-4

**DEPT. OF PHARMACOLOGY**  
**VISUAL ANALOGUE SCALE**

**(A) INSTRUCTIONS**

1. These three scales have opposite mood related adjectives at each end.
2. The scale is 100 mm in length. The midpoint of scale which is marked indicate your normal state.
3. Mark (X) the current state of your feelings on each of these scales, at any one point.

Vol. No. \_\_\_\_\_

**(B) WORKING SECTION**

Wide  
awake

Alert

Ability to  
concentrate

Extremely  
sleepy

Dull

Inability to  
concentrate

scales were used. The volunteers were asked to indicate the state of their feelings by making appropriate marks on a 100 mm horizontal line (Photograph-4). The scale has opposite mood related adjectives at each end and the midpoint of each scale was taken as normal state. The dimensions were- (VAS-1) wide awake - extremely sleepy, (VAS-2) alert- dull and (VAS-3) ability to concentrate- inability to concentrate.

## Statistical analysis of data

Unpaired 't' test was applied using Prism software, version 5.03 (Trial) for the analysis of data.

## Results

Chlorpheniramine increased the errors significantly at 2 hours and 4 hours in SDCT (Table-1) while placebo did not affect the score significantly at both time intervals. Chlorpheniramine decreased the digit symbol substitution score on DSST at both time intervals (Table-1) while placebo did not decrease the scores significantly at both time intervals. Chlorpheniramine reduced the arithmetic ability score suggestive of impairment of central processing ability (Table-1) but placebo did not impair (Table-1). In subjective test, chlorpheniramine caused

significant shift of the visual analogue scales towards extremely sleepy, dull and inability to concentrate end (Table-1).

## Discussion

In the study chlorpheniramine in comparison of placebo impaired performance on all the objective paper pencil tests which was correlated with their state of feelings on the subjective scales. The findings were expected because chlorpheniramine is an alkylamine compound and is lipophilic in nature. The ability of chlorpheniramine to penetrate blood-brain barrier is related to its lipophilicity and relatively low molecular weight hence crosses the blood-brain barrier readily. The mechanism by which it produces sedation and consequently the decremental effects on psychomotor performance is blockade of central  $H_1$ -receptors which are known to induce wakefulness<sup>13</sup>. The other mechanism by which chlorpheniramine produce sedation is that it blocks central muscarinic and serotonin receptors.<sup>14</sup> The psychomotor impairment by chlorpheniramine is also seen in the studies of Clarke et al<sup>15</sup> who found impairment with chlorpheniramine 4 mg on visuo-motor coordination and on visual analogue scale 1.5hrs after drug administration and Meador et al<sup>16</sup> in which they observed that chlorpheniramine 8mg prolonged the latency of P3-evoked potential and impaired performance on visual analogue scale three hours post drug administration.

Thus the sedative effect of chlorpheniramine leading to psychomotor impairment is well known. In other words it can be inferred that paper pencil tests are sensitive to detect the psychomotor impairment caused by chlorpheniramine. This is in concurrence with the study of Stone<sup>5</sup> who reviewed the literature on pencil and paper tests and concluded that pencil and paper tests are useful for detecting psychomotor performance and letter cancellation, arithmetic, DSST are most sensitive tests. Moreover paper pencil test of visual analogue scales to assess subjective component was also impaired. This

**Table 1:** Effect of chlorpheniramine and placebo on paper pencil tests at 2 hours and 4 hours.

Test	Chlorpheniramine Std. Dev N=24	Placebo Std. Dev N=24	Difference between means	95% confidence interval	t value df=46	P value
SDCT 2 Hrs	31.55	30.61	-21.17 ± 8.974	-39.25 to -3.087	2.359	0.0226*
SDCT 4 Hrs	31.89	31.25	-35.38 ± 9.115	-53.74 to -17.01	3.881	0.0003*
DSST 2 Hrs	18.74	18.81	-44.79 ± 5.420	-55.71 to -33.87	8.264	< 0.0001*
DSST 4 Hrs	21.94	19.53	-52.37 ± 5.997	-64.46 to -40.29	8.733	< 0.0001*
AA 2 Hrs	1.504	1.742	-3.917 ± 0.4698	-4.863 to -2.970	8.337	< 0.0001*
AA 4 Hrs	1.454	1.613	-4.042 ± 0.4433	-4.935 to -3.149	9.118	< 0.0001*
VAS1-2 Hrs	4.773	10.29	-16.04 ± 2.315	-20.70 to -11.38	6.931	< 0.0001*
VAS1-4 Hrs	6.753	10.18	-28.13 ± 2.494	-33.15 to -23.10	11.28	< 0.0001*
VAS2-2 Hrs	7.587	9.925	-24.17 ± 2.550	-29.30 to -19.03	9.477	< 0.0001*
VAS2-4 Hrs	8.877	10.5	-27.92 ± 2.806	-33.57 to -22.26	9.949	< 0.0001*
VAS3-2 Hrs	10.56	11.13	-20.63 ± 3.132	-26.94 to -14.31	6.585	< 0.0001*
VAS3-4 Hrs	11.95	12.7	-27.92 ± 3.560	-35.09 to -20.74	7.842	< 0.0001*

correlates with the study of Maxwell<sup>17</sup> who evaluated the sensitivity and accuracy of the visual analogue scale by a psycho-physical classroom experiment.

Coordination between sensory, motor system along with central integration and processing is required for psychomotor performance. The three levels of sensory information processing are detection, perception, and recognition. The drugs can affect at any of these levels and may hamper psychomotor performance. The perception component can be assessed by using a letter or number cancellation task like six digit cancellation test. In sensory recoding and processing identification and matching of current information with previously stored is done and this is assessed by digit symbol substitution test. Central processing which is an important function of central nervous system is evaluated by arithmetic or number handling task. Moreover psychomotor drugs can act upon mood, feeling and state of awareness of subjects. Thus both objective measurement and subjective rating are important in obtaining information of the effects of drugs on psychomotor functions.<sup>18</sup>

## Conclusion

It can be concluded from the study that paper and pencil tests are most economical, simple to perform and do not require sophisticated instruments hence they are useful tools for the assessment of psychomotor performance. Paper and pencil test can also be used as preliminary psychometric tests to rule out psychomotor impairments in Indian population of all drugs with CNS effects which are launched in India. Other objective tests involving complicated instruments or simulation can be followed if the drug detects psychomotor impairment by paper and pencil test. Moreover we can also give simple projects involving paper pencil tests to MBBS students to stimulate their appetite of research.

## References

1. Kamei, H., Noda, Y., Ishikawa, K., Senzaki, K., Muraoka, I., Hasegawa, Y., Hindmarch, I., Nabeshima, T. Comparative study of acute effects of single doses of fexofenadine, olopatadine, d-chlorpheniramine and placebo on psychomotor function in healthy volunteers. *Hum Psychopharmacol* 2003 ; 18(8) : 611-8.
2. Broadbent, D.E. Performance and its measurement. *Br J Clin Pharmacol* 1984 ; 18 : 55-95.
3. Nicholson, A.N. Concluding remarks (International seminar on psychotropic drugs and performance measurement). *Br J Clin Pharmacol* 1984 ; 18 : 139S-140S.
4. Manual on Clinical Pharmacology. Workshop on clinical pharmacology, 2003. Post Grad 1st Med Ed Res (PGIMER) Chandigarh.
5. Stone, B.M. Pencil and Paper tests-sensitivity to psychotropic drugs. *Br J Clin Pharmacol* 1984 ; 18 Suppl 1 : 155-205.
6. Chong, D., Wong, C.K., Ong, H.T., Lee, C.Y., Lee, B.W., Shek, L.P. Central nervous system side effects of first and second generation antihistamines in school children with perennial allergic rhinitis: a randomized double blind, placebo-controlled comparative study. *Pediatr* 2004 ; 113(2) : 116-21.
7. Philpot, E.E., Brooker, A.E., Biegalski, C.S. Effects of sedating and non-sedating antihistamines on flying performance. *Mil Med* 1993 ; 158(10) : 654-60.
8. Witek, T.J. Jr., Canestrari, D.A., Miller, R.D., Yang, J.Y., Riker, D.K. Characterization of daytime sleepiness and psychomotor performance following H<sub>1</sub> receptor antagonists. *Ann Allergy asthma Immunol* 1995 ; 74(5) : 419-426.
9. Waller, D., Levander, S. Smoking and vigilance. The effect of tobacco smoking on CFF as related to personality and smoking habits. *Psychopharmacology (Berl)* 1980 ; 70(2) : 131-6.
10. Hindmarch, I., Rigney, U., Stanley, N., Quinlan, P., Raycroft, J., Lane, J. A naturalistic investigation of the effects of day-long consumption of tea, coffee and water on alertness, sleep onset and sleep quality. *Psychopharmacology (Berl)* 2000 ; 149(3) : 203-16.
11. Hindmarch, I., Quinlan, P.T., Moore, K.L., Parkin, C. The effects of black tea and other beverages on aspect of cognition and psychomotor performance. *Psychopharmacology (Berl)* 1998 ; 139(3) : 230-8.
12. Aitken, R.C.B. Measurement of feelings using visual analogue scales. *Proc Roy Soc Med* 1969 ; 62 : 989-993.
13. Brown, N.J., Roberts, L.J. Histamine, Bradykinin and their antagonists. In: Hardman, J.G., Limbird, L.E., Molinoff, P.B., Ruddon, R.W., Gillman, A.G., editors, Goodman and Gilman's The pharmacological basis of therapeutics 10<sup>th</sup> International edition, New York, McGraw - Hill, 2001 : 645-658.
14. Simons, F.E., Reggin, J.D., Roberts, J.R., Simons, K.J. Benefit/risk ratio of the antihistamines (H<sub>1</sub>-receptor antagonists) terfenadine and lorpheniramine in children. *J Pediatr* 1994 ; 124(6) : 979-83.
15. Clarke, C.H., Nicholson, A.N. Performance studies with antihistamines. *Br J Clin Pharmacol* 1978 ; 6 : 31-35.
16. Meador, K.J., Ioring, D.W., Thompson, E.E., Thompson, W.O. Differential cognitive effects of terfenadine and chlorpheniramine. *J Allergy Clin Immunol* 1989 ; 84(3) : 322-325.
17. Maxwell, C. Sensitivity and accuracy of the visual analogue scale: A Psycho-physical classroom experiment. *Br J Clin Pharmacol* 1978 ; 6 : 15-24.
18. Hindmarch, I. Psychomotor function and Psychoactive drugs. *Br J Clin Pharmacol* 1980 ; 10 : 189-209.



# The psychomotor effects of levocetirizine- a second generation antihistamine in healthy volunteers

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## Abstract

Levocetirizine, six digit cancellation test, psychomotor performance.

## Background

Levocetirizine, a new second generation antihistamine which is claimed to be non-sedative in western studies is an R-enantiomer of cetirizine. In Indian context there is little literature available about its impact on psychomotor performance. That's why present study was planned to exclude the possibility of adverse effect of levocetirizine on psychomotor performance in Indian conditions.

## Materials and methods

In this double blind, placebo controlled, cross over study, 24 healthy volunteers performed various objective and subjective psychometric test after single dose of levocetirizine 5 mg, chlorpheniramine 4 mg or placebo at 0hrs, 2hrs and 4 hrs intervals. The test battery included was - six digit cancellation test, digit symbol substitution test, arithmetic ability, critical flicker fusion, serial verbal learning, hand steadiness test and three different visual analogue scales.

## Results

In the present study levocetirizine was statistically similar with chlorpheniramine on six digit cancellation test (p value <0.05), however it did not impair any other psychomotor performance test and was similar to placebo. Chlorpheniramine impaired performance significantly on all the objective and subjective psychomotor test at both time intervals.

## Conclusion

It can be concluded that levocetirizine in 5mg dose is free from the negative effects of the previous generation of antihistamines and do not impair psychomotor performance in Indian conditions also.

## Keywords

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## Introduction

Allergic conditions have a significant impact on quality of life. Allergic condition such as allergic rhinitis is common. In the US, for example, allergic rhinitis is considered to affect 10-30% of adults and upto 40% of children, and to account annually for about 5.5 million days of absence from school or work.<sup>1</sup> In 1937 the first histamine receptor antagonist was discovered for the management of allergic disorders.<sup>2</sup> In few decades these therapeutic agents have emerged as one of the most widely used classes of drugs in world.<sup>3</sup> Today, many antihistamines are available but older generation often cause adverse effects, particularly psychomotor and cognitive. It leads to patient maladjustment and may impair psychomotor performance, which plays important role in driving and operating complex machinery.

Levocetirizine, a new second generation antihistamine which claimed to be non sedative<sup>4</sup> in western studies is an R-enantiomer of cetirizine. Levocetirizine 5mg is significantly superior to placebo and at least equally efficient in the relieving allergic symptoms as cetirizine in its recommended dose (10mg)<sup>4</sup> but positron emission tomography (PET) measurement revealed that about 30% of brain H<sub>1</sub>-receptor were occupied by cetirizine<sup>5</sup> which are concerned with wakefulness. In this context the present study was planned to exclude the possibility of adverse effect of levocetirizine on psychomotor performance in India.

## Materials and methods

In this double blind, placebo-controlled, cross-over study, sample size of 24 was calculated at the level of significance  $\alpha = 5\%$  and power 80% by the statistician. Twenty four healthy volunteers aged between 18 to 20 years were included in the study after taking informed written consent and excluding general and systemic abnormality. Ethical approval was obtained from the Institutional Ethics committee.

Before beginning the study, the subjects were explained about the experimental procedures and the psychomotor function tests. The volunteers received training till a performance plateau was reached with the battery of psychomotor tests to avoid learning curve effect. Each of



the volunteer acted as his own control and each volunteer got each formulation by making cross over. The total period of the study was 4 weeks for each volunteer with a washout period of one week between any two of the drugs. Following each single dose of levocetirizine 5 mg, chlorpheniramine 4 mg or placebo, subjects performed a series of psychomotor performance tests at 0 hours, 2 hours and 4 hours post dose. Various objective tests performed by the volunteers were six digit cancellation test (SDCT)<sup>6</sup>, digit symbol substitution test (DSST)<sup>6</sup>, arithmetic ability (A.A.)<sup>7</sup>, critical flicker fusion (CFFT)<sup>8</sup>, serial verbal learning (SVL)<sup>9</sup> and hand steadiness test (HST)<sup>9</sup> for measurement of sensory, central nervous and motor components, and subjective tests such as three different visual analogue scales (VAS)<sup>10</sup>. The pharmacokinetic of the drugs were taken into account when deciding the test times. Chlorpheniramine was included in the study as positive internal control.

Perception (sensory component) was evaluated by SDCT in which subject had to cancel as many target digits as possible within 2 minutes time period of a sheet of 1200 randomized digits arranged in 40 columns by six digit key. While recognition (sensory component) was evaluated by DSST in which the subjects were required to insert a symbol above each digit during 2 minutes time period for odd, even and zero numbers on a given sheet of 200 randomized digits.

Central processing was assessed by arithmetic ability test, in which simple mathematical problems like addition, subtraction had to be solved during 2 minutes duration. CFFT was used to evaluate integration by using critical flicker fusion apparatus in which mean of both fusion and flicker was found. While short term memory was tested by SVL test using memory drum apparatus in which the list

of 10 non-sense syllables were shown one by one for 2 second and were given 20 seconds to recall serially without any error.

For evaluation of motor component, HST was performed by the subjects using steadiness tester - a device with a series of holes of varying size, a stylus and digital counter. The subject has to insert the stylus into the hole without touching the sides within 15 seconds and error time was noted.

For subjective component, three different visual analogue scales used with opposite mood related adjectives at each end. The dimensions were- (VAS-1) wide awake - extremely sleepy, (VAS-2) alert- dull and (VAS-3) ability to concentrate- inability to concentrate. The midpoint of each scale was taken as normal state. The volunteers were asked to indicate the state of their feelings by making marks on the scale.

For comparison within drug, paired 't' test was applied using Prism software, version 5.03 (Trial). While one way ANOVA was applied for comparison in between the drugs using Microsoft Office Excel 2007.

## Results

In SDCT (table-1) levocetirizine and chlorpheniramine increased the errors significantly at 2 hrs and 4 hrs while placebo did not affect the score significantly. Chlorpheniramine decreased the substitution of symbols score on DSST at both time intervals (Table-1) while levocetirizine and placebo did not decrease the scores significantly (Table-1) and were statistically similar at both time intervals (Table-3). Chlorpheniramine reduced the CFFT threshold and arithmetic ability score suggestive of impairment of central integrative capacity and central

**Table 1:** Effects of levocetirizine and chlorpheniramine at 2 hours and 4 hours.

Mean ± S.E.M				
Test	Drug	0 HR	2HR	4HR
SDCT	Chlorpheniramine	146.3+ 7.53	118.7+6.44*	104.5+6.51*
	Levocetirizine	145.10+7.75	124.40+3.16*	114.00+3.16*
	Placebo	138.80+7.03	139.80+6.25	139.90+6.38
DSST	Chlorpheniramine	128.3+5.25	89.29+3.83*	82.33+4.48*
	Levocetirizine	132.70+4.38	131.50+4.53	130.40+4.39
	Placebo	135.40+4.37	134.10+3.84	134.70+3.99
AA	Chlorpheniramine	9.708+0.56	6.00+0.31*	5.875+0.30*
	Levocetirizine	9.83+0.45	9.88+0.41	9.75+0.41
	Placebo	9.88+0.35	9.92+0.36	9.92+0.33
CFFT	Chlorpheniramine	35.96+0.54	25.79+0.76*	22.92+1.23*
	Levocetirizine	35.25+0.88	34.88+0.62	34.33+0.48
	Placebo	35.13+0.90	35.33+0.99	35.08+1.16
SVL	Chlorpheniramine	3.208+0.08	5.042+0.16*	6.625+0.23*
	Levocetirizine	3.13+0.09	3.17+0.10	3.25+0.11
	Placebo	3.25+0.09	3.29+0.09	3.46+0.10
HST	Chlorpheniramine	682.9±53.42	1157±50.82*	1323±80.98*
	Levocetirizine	675.90±68.58	634.30±74.92	645.50±75.75
	Placebo	673.50±68.30	660.80±62.75	662.10±65.86

\* Indicates p value less than 0.05 (P<0.05)

**Table 2:** Effects of levocetirizine and chlorpheniramine at 2 hours and 4 hours.

Mean ± S.E.M				
Test	Drug	0 HR	2HR	4HR
VAS-1	Chlorpheniramine	85.42±1.56	69.79±0.97*	56.04±1.38*
	Levocetirizine	85.63±2.45	84.17±2.46	82.50±2.33
	Placebo	86.25±1.68	85.83±2.10	84.17±2.08
VAS-2	Chlorpheniramine	83.96±2.11	61.46±1.55*	56.25±1.81*
	Levocetirizine	85.83±2.23	85.63±1.71	85.21±1.77
	Placebo	86.88±1.27	85.63±2.03	84.17±2.14
VAS-3	Chlorpheniramine	86.04±2.02	64.38±2.16*	55.83±2.44*
	Levocetirizine	83.75±2.36	84.58±2.37	83.13±2.17
	Placebo	84.38±2.03	85.00±2.27	83.75±2.59

**Table 3:** Table showing inter drug comparison between levocetirizine, chlorpheniramine and placebo with one way ANOVA test.

Time	2 Hours	4 Hours	2 Hours	4 Hours
Test	F value	P value	F value	P value
SDCT	3.97	0.0232	10.80	0.0001
DSST	38.02	0.0001	45.89	0.0001
AA	39.07	0.0001	42.67	0.0001
CFFT	44.57	0.0001	45.31	0.0001
SVL	72.07	0.0001	140.76	0.0001
HST	21.43	0.0001	26.93	0.0001
VAS1	20.48	0.0001	64.10	0.0001
VAS2	61.94	0.0001	73.62	0.0001
VAS3	27.04	0.0001	43.89	0.0001

processing ability respectively (Table 1) but levocetirizine and placebo were similar without any impairment (Table 1 & 3). Chlorpheniramine (Table-1) significantly increased SVL score suggestive of impairment of short term memory and in HST increased errors significantly at 2hrs as well as at 4 hrs but other two didn't have any significant effect on both time intervals (Table 1 & 3). These findings of chlorpheniramine on objective tests were also reflected in the subjective assessment of visual analogue scale VAS -1, VAS-2 and VAS-3 with a significant shift of the scale towards extremely sleepy, dull and inability to concentrate (Table 2). Chlorpheniramine when compared to levocetirizine and placebo had shown significant impairment on objective and subjective tests at both time intervals except in SDCT where it was similar to levocetirizine (Table 3).

## Discussion

In the present study levocetirizine shown similarity with chlorpheniramine on SDCT, however it did not impair any other psychomotor performance test and was similar to placebo. Detection, perception and recognition of a stimulus are three levels of information processing which together account for the majority of sensory activity. In the CNS, analysis of sensory stimulus occurs which ultimately produces coordinated behavioural response. Perceptual processing of sensory information can be influenced by personality and individual motivation<sup>6</sup>. So the possible

reason for this differential effect may be due to personality and environmental changes because SDCT is a measure of attention (perceptual processing of sensory information).

Hindmarch et al<sup>11</sup> found that 5mg levocetirizine had no effect on critical flicker fusion test. These findings of objective tests were correlated with subjective rating scales for sedation. In the study of Gandon and Allain<sup>12</sup>, it was found that 5mg levocetirizine did not modify the critical flicker fusion test and learning memory was not affected. Verster et al<sup>4</sup> in their study opined that acute and sub chronic doses of levocetirizine did not impair memory functioning and psychomotor performance. Our findings (in Indian scenario) are in accordance to above mentioned western studies.

Chlorpheniramine impaired all psychomotor performance tests which are in accordance to the various previous studies of Clarke and Nicholson<sup>13</sup>, Meador et al<sup>14</sup>, Khosla et al<sup>15</sup> and Simons et al<sup>16</sup>. Our study also confirms that it impairs psychomotor performance.

## Conclusion

It can be concluded from the study that in Indian population and environment, levocetirizine at normal therapeutic dose of 5mg does not impair psychomotor performance and is free from the negative effects of the older generation of antihistamines and so should prove valuable in the treatment of allergic disorders. But large scale postmarketing surveillance studies will only provide exact nature of its behaviour in the Indian population.

## References

1. Murdoch, D., Goa, K.L., Keam, S.J. Desloratadine An update of its efficacy in the management of allergic disorders. *Drugs* 2003; 63 (19): 2051- 2077.
2. Slater, J.W., Zechnich, A.D., Haxby, D.G. Second - generation antihistamines a comparative review. *Drugs* 1999; 57 (1): 31-47.
3. Lawrence, M., Buske, D. Clinical comparison of histamine H<sub>1</sub> - receptor antagonist drugs. *J Allergy Clin Immunol* 1996; 98 (6 pt 3): S 307 – S318.
4. Verster, J.C., Volkerts, E.R., van Oosterwijck, A.W., Arab, M., Bijtjes, S.I., De Weert, A.M., Eijken, E.J., Verbaten,

- M.N. Acute and subchronic effects of levocetirizine and diphenhydramine on memory functioning, psychomotor performance, and mood. *J Allergy Clin Immunol* 2003 ;111(3) : 623-7.
5. Tashiro, M., Mochizuki, H., Iwabuchi, K., Sakurada, Y., Itoh, M. Roles of histamine in regulation of arousal and cognition: functional neuroimaging of histamine H<sub>1</sub> – receptor in human brain. *Life Sci* 2002 ; 72 : 409-414.
  6. Manual on Clinical Pharmacology. Workshop on clinical pharmacology, 2003. Post Grad 1<sup>st</sup> Med Ed Res (PGIMER) Chandigarh.
  7. Stone, B.M. Pencil and paper tests-sensitivity to psychotropic drugs. *Br J Clin Pharmacol* 1984; 18 Suppl 1: 15S-20S.
  8. Manual Pharmatech. Techniques in pharmacology. Seth GS Med Coll and KEM Hosp Mumbai 1996.
  9. Marshall, S., Colon, E.A. Effects of allergy season on mood and cognitive functions. *Ann Allergy* 1993; 71: 251-258.
  10. Aitken, R.C.B. Measurement of feelings using visual analogue scales. *Proc Roy Soc Med* 1969; 62: 989-993.
  11. Hindmarch, I., Johnson, S., Meadows, R., Kirkpatrick, T., Shamsi, Z. The acute and sub-chronic effects of levocetirizine, cetirizine, loratadine, promethazine and placebo on cognitive function, psychomotor performance, and wheal and flare. *Curr Med Res Opin* 2001; 17 (4): 241 – 55.
  12. Gandon, J.M., Allain, H. Lack of effect of single and repeated doses of levocetirizine, a new antihistamine drug, on cognitive and psychomotor function in healthy volunteers. *Br J Clin Pharmacol* 2002; 54: 51-58.
  13. Clarke, C.H., Nicholson, A.N. Performance studies with antihistamines. *Br J Clin Pharmacol* 1978 ; 6 : 31-35.
  14. Meador, K.J., Ioring, D.W., Thompson, E.E., Thompson, W.O. Differential cognitive effects of terfenadine and chlorpheniramine. *J Allergy Clin Immunol* 1989; 84(3): 322-325.
  15. Khosla, P.P., Saha, N., Koul, A., Chakrabarti, A., Sankarnarayanan, A., Sharma, P.L. Effects of ranitidine alone and in combination with chlorpheniramine on histamine-induced wheal and flare and psychomotor performance. *Indian J Physiol Pharmacol* 1993; 37(2): 132-4.
  16. Simons, F.E., Reggin, J.D., Roberts, J.R., Simons, K.J. Benefit/risk ratio of the antihistamines (H<sub>1</sub>-receptor antagonists) terfenadine and chlorpheniramine in children. *Pediatr* 1994; 124(6): 979-83.

# Assessment of the attitudes of clinicians in the emergency setting towards an act of parasuicide

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## Abstract

## Objective

This study was conducted to know the prevailing common attitudes of clinicians in an emergency setup towards patients attempting suicide.

## Method

A 34 item questionnaire which has been used in a previous similar study was used. The data was subjected to factor analysis.

## Results

showed marked rejection, avoidance, hostility and indifference was found. Conclusion- various internal and external factors, interact to produce the negative attitude in the clinicians. The need for the better training, holistic and multidisciplinary approach is the call of the recent times.

## Keywords

Suicide, DSH(Deliberate Self Harm), Clinicians attitudes, emergency setting

## Introduction

In the past two to three decades suicide has emerged as one of the leading causes of death(WHO-2001). Multiple factors like biological, sociological and psychological interact leading to an act of completed suicide(Beautrais,Joyce et.al-1996). For every completed suicide 8-10 cases of parasuicide occur(WHO-2001)All such cases report to the emergency setting of a hospital.The burden of evaluation, primary intervention and future referral, all fall on the personnel working in the emergency setup(McCann,Eileen et.al-2006 ). Multiple factors which can be external like workload, long hours, lack of facility and overloading can interfere with the management and evaluation by the emergency staff. Internal factors like rejection, anxiety, feelings of inadequacy and hostility also interfere in optimal management strategies(Dressler-1975). The above factors make a patient of deliberate self harm (DSH) unpopular in the eyes of the first care givers in the emergency staff. To ensure that the rejection, hostility and indifference do not interfere with the referral and future management, a change in attitude is necessary. The

ever increasing numbers of suicide attempters (Who-2001), make it imperative that the problem be addressed on a priority basis. The attitudes which determine enthusiasm in treatment are important because it affects the treatment efficacy(Patel-1975). The training of an average medical personnel casually addresses the aspect of suicide(Ramon,Bancroft,Skirmswire-1975). Not much importance is given to address this significant aspect. The above factors and lack of data related to this particular region of India have prompted the present study.

## Methodology

The present study was carried out in Sir Sunder Lal hospital at Institute of Medical Sciences Banaras Hindu University, Varanasi, India. This is a nodal hospital which caters to a large population belonging to three neighbouring states, namely Bihar, Uttar Pradesh, Jharkhand. The hospital is also a referral centre. The majority of attempted suicide are attended in the emergency section. 100 doctors who were attending the emergency patients, were chosen for the study. The doctors belonged to multiple specialities like general medicine, surgery, anaesthesia and neurology. These clinicians are usually the front line clinicians dealing with suicidal behaviour. All the doctors posted over the span of three months were included. A 34 item questionnaire with yes/no as response was administered. These questionnaires were used in a previous study conducted in India (Sethi and Uppal-2006). Since the response to questionnaire is in a 'yes' and 'No' format a factor analysis approach was considered. A response of 'Yes' does not exactly mean a 'No' in that area and vice versa.

## Results

In this study six factors were seen to explain the maximum variance of 46.5% as shown in table 1. Only seven items were loaded towards one factor. The main reason for negative attitude were the involvement in medico legal issues and the perception that the patient of suicide is a drain on the resources and an act of cowardice. Six items were loaded on factor two that dealt with indifference towards the suicide attempter. The clinicians admitted to the need for support, care and feeling of helplessness in dealing with such patients. Five items were loaded in factor three. There was however, a significant proportion of clinicians who felt that a need for intervention was a must for the patient and his/her family. The clinicians were seen

to be ambivalent regarding their own need for ventilation and anxiety reduction. Five items were loaded on factor four which indicates clinicians attitude of rejection, hostility, avoidance as well as considering attempted suicide patients as nuisance for medical services. Four items were loaded in factor five and six are suggestive of clinicians' positive view for suicide attempters, accepting suicidal act as a part of mental illness and the need for some professional help (Table II). Fig 1 shows a graphic representation of the varimax rotation. Four factors have maximum rotation.

## Discussion

The study gives evidence for the negative attitudes of clinicians. In an emergency setup, such an attitude can have a poor prognostic implication (McCann, Eileen et al - 2006). A patient of deliberate self harm (DSH) is in a vulnerable state of mind, being confronted with a rejecting clinician can drive the individual to desperation. Multiple external factors like workload, lack of training medicolegal hassles' are contributory to this attitude (Dressler-1975). Internal factors like lack of exposure, ones own anxieties and state of mind also come into play. Our findings are different from the findings of a similar study using the same methodology (Sethi and Uppal-2006). We opine that the reason could be the geographical position and the sociocultural background. Our hospital caters to comparatively illiterate and predominantly rural background population. Dealing with a large population of illiterate and relatively unaware mass, makes a clinician unwilling to do the 'talk therapy'.

Using a visual analogue scale researchers have made conclusions pointing towards a negative, rejecting attitude (Goldney-1998), using a semantic differential method authors have shown that all emergency room personnel (clinicians, nurses and paraclinical staff) had an unsympathetic attitude towards patients of DSH (Ramon et al. 1975). Employing a 41 item questionnaire and factor analysis and comparing the doctors attitude to that of nurses it was found that the nurses were more accepting of the parasuicidal patient. Clinicians on the other hand gave responses of "I fail to understand" "manipulative" "bothersome". McCann et al. showed that experienced older nurses were more sympathetic and understanding, they also found that clinicians in the ward were more accepting than the emergency room clinicians. In a more serious fashion Patel-1975 have shown that during a crisis the patient does not contact the family physician, as the doctors are perceived as unhelpful by the suicidal patient. In our study the factor of rejection and indifference support the above view point. Chiles and Strosahl-1989 showed that the starting 50% of suicide attempters did not use the average medical help. This figure can be markedly reduced by simple manipulations in training and education of clinicians (Diekstra-1989).

Our study also points out that the law serves the purpose of a deterrent. As suicide is an act punishable by law,

cumbersome legal procedures, court summons and unnecessary paper work, make clinicians avoid dealing with such patients e.g. factor III.

An important aspect of one's own feelings and anxiety in dealing with death cannot be ignored. Clinicians dealing with such patients can be reminded about their own mental health, frustrations and aspirations. The feeling of guilt helplessness and inadequacy can also lead to a reaction formation of hostility, anger and ambivalence (McCann, Eileen et al - 2006). The stressful life of trainee clinicians, who constitute the bulk of emergency room clinicians, serves as a contributory factor for the unempathetic attitude. The perception of psychiatric help seeking as being weakness of self and will also help in strengthening the stigma associated with treatment. The

**Table 1: Total Variance Explained**

Component	Initial Eigenvalues			Rotation Sums of Squared Loadings		
	Total	% of Variance	Cumulative %	Total	% of Variance	Cumulative %
1	4.279	12.584	12.584	3.489	10.261	10.261
2	3.072	9.035	21.619	2.904	8.542	18.804
3	2.481	7.298	28.917	2.672	7.860	26.664
4	2.240	6.589	35.506	2.581	7.591	34.255
5	1.946	5.724	41.231	2.237	6.580	40.835
6	1.817	5.344	46.575	1.952	5.740	46.575
7	1.704	5.013	51.588			
8	1.481	4.356	55.944			
9	1.402	4.124	60.068			
10	1.238	3.640	63.708			
11	1.208	3.554	67.262			
12	1.037	3.050	70.312			
13	.941	2.767	73.079			
14	.914	2.689	75.769			
15	.810	2.383	78.152			
16	.778	2.288	80.440			
17	.672	1.975	82.415			
18	.622	1.828	84.244			
19	.580	1.704	85.948			
20	.531	1.562	87.510			
21	.524	1.542	89.052			
22	.465	1.368	90.420			
23	.454	1.335	91.755			
24	.430	1.265	93.020			
25	.400	1.175	94.195			
26	.306	.901	95.097			
27	.299	.881	95.977			
28	.255	.750	96.727			
29	.245	.721	97.448			
30	.215	.631	98.079			
31	.206	.606	98.685			
32	.167	.491	99.176			
33	.162	.475	99.651			
34	.119	.349	100.000			

Extraction Method: Principal Component Analysis.

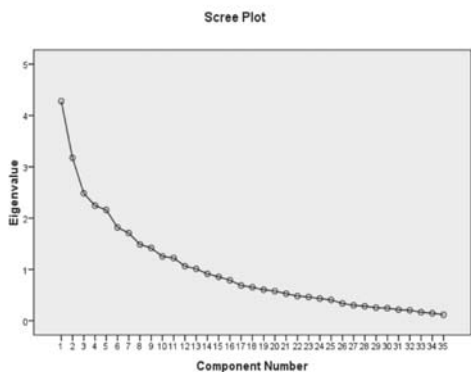
**Table 2:** Six-factor solution  
Rotated Component Matrix

Items of attitude	Component					
	1	2	3	4	5	6
need help	-.741					
Cowerdice	-.711					
medicolegal prob	.627					
ignore&left alone	.603					
sucide as courage	.578					
waste of	.549					
medical services						
need att&love						
society responsible		-.771				
negelect for ur part		.588				
increase sucide		.570				
disappointment		.529				
with pt.						
sucide prevention	-.418	-.508		-.401		
cry for help		-.422				
u feel fearful						
avoid responsibility						
uneasy working with victims			.708			
comfortable with attempter			-.690			
clinicians anxiety			.614			
victims need help			-.543			
remind sucidalthought			.532			
nuisance for medical						
punishable				.726		
make distance				.720		
sucide reason				-.619		
Does sucidal act bother u				-.472		
care for sucide						
help to feel better					.726	
help for urself					.662	
no difference to u					.562	
sinful act					.522	
make u angree						.727
mental illness						.518
sucide rightchoice at time						.449
personal himselr						

Extraction Method: Principal Component Analysis.

Rotation Method: Varimax with Kaiser Normalization. A Rotation converged in 11 iterations

**Figure 1:**



average clinician gets about a couple of hours of exposure to issues related to mental health, this further strengthens the shroud of mystery regarding psychiatric illness (Ramon,Bancroft et.al-1975).

The study results lead one to conclude that training of clinicians and sensitization can help to change the attitude and this can cause a willingness to assess and generate skills to deal with such patients(Patel-1975) . This change can help in future prognosis. Frequent attempters can be helped by this attitude(Goldney-1998) . Furthermore about 90% of people attempting suicide have one or more psychiatric diagnosis(Beautrais,Joyce et.al-1996), therefore timely referral can help save many lives. The common perception that a depressed patient has a loss of

“willpower” may be unfounded as an act of suicide can sometimes be a reinforced problem solving method which one can resort to(Lanny Berman-2009), hence the problem which the act of suicide addresses should be tackled first, this can be achieved by an attitude of empathy (Chiles,Strosahl-1989). A better communication with the mental health team, good referral pattern and streamlining the legal procedures can help in recognizing and responding to suicide risk(Lanny Berman-2009). This aspect is all the more important since attempted suicide increases the risk of completed suicide(WHO-2001).

## Conclusion

Multiple causes like depression ,anxiety disorders, personality disorders,substance abuse and schizophrenia can all lead to an increase in suicidal behaviour(Beautrais,Joyce et.al.-1996). Ever increasing number of patients of DSH should motivate the clinician community. The physician community itself is a vulnerable group. In tackling this problem we will be benefitting our own lot(Patel-1975). Death and dealing with it is a common practice with the clinicians , however confronting one’s own death thoughts can be a frightening and anxiety provoking experience. A change in attitude can go a long way in helping the patient population reach the right place for treatment and thus decrease the morbidity associated with mental illness. A multidisciplinary team and adequate personnel with active crisis intervention training can be of great help.

## Limitations and future suggestion of the study

Our study used a larger sample size and tried to replicate, the findings of a similar previous study from India(Sethi and Uppal-2006). The varimax factor rotation gave different results. Our major sample population was the resident clinician, who has multiple responsibilities both academic, clinical and research related,their preoccupation may be many hence their negative attitude . In addition their own frustrations regarding their academic and personal aspiration might interfere with their attitude. We could have looked at the gender differences between the respondents,assuming that females are more adept at handling and addressing emotional issues(Diekstra-1989). A comparison between mental health professions paraclinical staff like nurses and general clinicians can be undertaken. The importance of the present study lies in the fact that it advocates the need for training of emergency room clinicians in dealing with crisis such as suicide(Goldney-1998). In trauma centres apart from the physical aspects,psychological trauma should also be addressed.This goal can be achieved after optimal training of the clinical staff.

In this study methodological point of view suggests need to add a control group of mental health professionals so that we can understand to what extent mental health professionals’ attitude towards suicide attempters are different from non mental health professionals. Second important suggestion is the need to develop a comprehensive scale based on Gutman methods so that we can measure the degree of positive and negative attitude of clinicians towards suicide attempters .

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## References

1. World Health organization (WHO).Suicide prevention: emerging from darkness. Geneva: WHO; 2001. p22.
2. Sethi S, Uppal S. Attitude of clinicians in emergency room towards suicide. Internatinal journal of psychiatry in clinical practice 2006;10(3):182-5.
3. Patel A. Attitude towards self – poisoning. Br Med J 1975;ii: 426-30.
4. Goldney S. Attitude of patients who attempted suicide. Med J Australia1998;717-19.
5. Ramon S, Bankcroft MJ, Skrimswire AM. Attitudes towards self-poisoning among physician and nurses in general hospital. British journal of psychiatry 1975;127: 257-64.
6. McCann RN, Eileen C, McConnachie S, Harvey I. Accident and emergency nurses attitude towards patients who self harm.Journal of accident and emergency nursing 2006;14:4-10.
7. Diekstra RFW. Suicide and its prevention: the role of attitude and limitation.In Maris R, Platt S, Schanidt-ke A, Sonneck G,Editors. Suicide. Geneva(WHO) : Publishers Brill1;1989.
8. Lowenthal U. Suicide – The other side. Arch Gen Psychiatry 1976; 33:838-42.
9. Berman L.Recognizing and responding to suicide risk(RRSR)-Advanced training for clinicians. In proceeding of the suicide prevention conference; Jan2009; San-Diego.USA.
10. Chiles JA, Strosahl KD, Ping ZY, Michael MC. Depression, hopelessness & suicidal behaviour in Chinese & American psychiatric patients. American Journal of psychiatry1989;146:339-44.
11. Beautrais AI, Joyce PR, Mulder RT, Fergusson DM, Deavill BJ, Nightingale SK. Prevalence and co morbidity of mental disorders in persons making serious suicide attempts: A case control study. Am J Psychiatry 1996; 153:1009-14.

# Facial index in adult Indian Punjabi males Jat Sikhs and Banias

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## Abstract

### Introduction

Face is an entity that allow us to distinguish one person from another. It also permits distinctions between races, ethnic groups, sexes and even members of same family. Human face can be studied by means of natural science or more specifically by biological anthropology, which is scientific study of human biological characters. Many factors are responsible for the variation in the human's face viz hormonal, genetic heritage, sex environment and age.

### Aims and objectives

This research was conducted in view of the importance of anthropometric indices of the face in plastic and cosmetic surgery, forensic medicine and other allied clinical sciences.

### Material and methods

This cross-sectional study was set up to determine and compare the face shape in Jat Sikhs and Bania males of Indian Punjab origin (300 adult male Jat Sikhs and 300 adult male Banias). The total facial height & breadth of bizygomatic arch were measured and the facial index was calculated. Then these two endogamous groups were compared for these parameters.

### Results

The dominant type of face shape in Jat Sikhs males was euryprosopic (39.94%) whereas hypereuryprosopic type of face was in dominance (44.51 %) in Bania males.

### Conclusion

This study showed that ethnicity can affect the form of face in adult Indian Punjabi male Jat Sikhs and Banias.

### Keywords

Facial Anthropometry, Facial Index, Adult Jat Sikh males, Bania males, Punjab

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## Introduction

When we look at a person, is not our attention generally focused on his or her lips, eyes, eyebrows, and hair? Yet these are merely the adornment for the basic facial framework. What really determines the extent of a person's attractiveness is the skeletal mass of the face, the configuration of its bones, and the unique volumetric form they create. The skin and subcutaneum are "canvas of the face" [1]. Face permits distinction between races, ethnic groups, sexes and even members of the same family [2].

The face is the body part that epitomises a human person. The face is required for identification of individuals in passports, on driving licenses and other documents. Yet the human face is an anatomical entity that arose through biological processes during the course of human evolution and its structure is regulated by the same embryological, anatomical and physiological mechanisms that form all other parts of the body. Thus the face can be studied by means of natural sciences or more specifically by biological anthropology, which can be defined as the scientific study of human biological characters [3].

Slight modifications in the structural elements of the face (bones, muscles, cartilage, adipose tissue) allow individual features or facial morphology to be superimposed over the general, modern human face pattern. These variations in facial morphology arise through differential growth, and create an individual face that allow us to distinguish one person from another. These variations are controlled by a number of factors viz hormonal, genetic heritage and the climate or environment. The combination of all of these influences produce slight modification in size and shape of different part of the face, which result in the development of a unique, recognisable visage. Even with in the same population, variation of facial features is considerable [3].

Facial measurements are affected by various parameters including age, sex, socioeconomic factor and environment. Since age ceases to affect the facial parameters in subjects above 18 years of age, this factor could be eliminated as a variable in craniofacial measurement. Ethnicity is a variable which affects facial features, a fact not sufficiently explored in India [4].

Anthropometric variations in different races or in isolated tribal communities in a country are well known. Indian society has a unique caste system. Due to strict endogamous caste system, the genetic pattern of the members may be well preserved. The occupation in India



has been determined by the caste of the individual. The Jats have been engaged in farming whereas the Baniyas constitute the business community. Thus in generations, the exposure to hot climate has been far greater in the Jats than Baniyas. These factors may possibly be responsible for the difference in the anthropometric measurements in the two communities [5].

The present day population of Punjab is composed of a number of endogamous groups, usually based on occupation. The major Punjabi communities are Jat Sikhs (dominant community), Baniyas, Brahmins, Khatri Aroras, Sainis and large number of backward and scheduled caste communities [6].

## Aims and objectives

The aim of the present study was to establish and compare basic facial anthropometric data of Jat Sikhs and Bania males of Indian Punjab origin and to recognize or establish applied significance of observations of present study to forensic, plastic and cosmetic surgery and other allied clinical sciences.

## Material and methods

The present study was based on study of facial anthropometry of 300 adult male Jat Sikhs and 300 adult male Baniyas of Punjab of Indian origin. Prior consent for this study was obtained from the subject. The sample was taken from both urban and rural habitation areas. Subjects were not chosen on the basis of bodily structure and proportion.

Care was taken to avoid measurements of related individuals and to exclude persons with apparent physical deformities. The methodology for anthropometric measurements was adopted from Singh and Bhasin (1968) [7].

The landmarks were marked on body by skin marking pencil. The head of subject was at rest without any strain in the eye-ear plane or Frankfurt-Horizontal Plane i.e. trignon and the infra orbitale were lying in the same horizontal plane.

## Somatometric landmarks and facial measurements

**1. Nasion (n) :** It is the point on the nasal root intersected by mid-sagittal plane. Nasal root is not the depression of the nose but at the nasofrontal suture which can be felt by slightly probing the root of the nose.

**2. Gnathion (gn) :** It is the lowest point on the lower margin of the lower jaw intersected by the mid-sagittal plane. This point can be palpated on the lower jaw slightly anterior to chin.

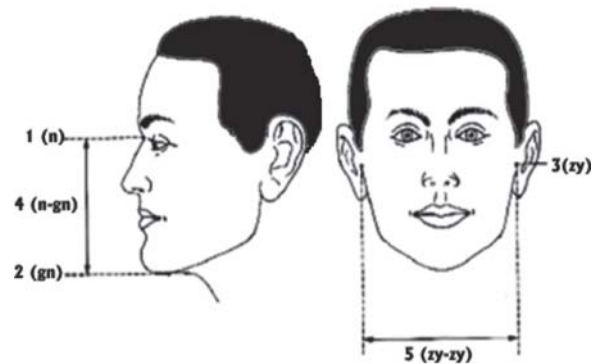
**3. Zygion (zy) :** It is the most laterally placed point on the zygomatic arch

**4. Morphological Facial Height or Total Facial Height**

**(n-gn):** It measures the straight distance between nasion (n) and gnathion (gn) by sliding caliper (figure 1).

**5. Breadth of Bizygomatic Arch (zy-zy):** It measures straight distance between the two zygion (zy) i.e. the most lateral points on the zygomatic arch by spreading caliper

**Figure 1** Sketch show (a) how the facial length and bizygomatic breadth were measured 1: nasion; 2: nathion; 3: zygoma; 4: total facial height; 5: breadth of bizygomatic arch



(figure 1). The greatest breadth of bizygomatic arch is usually found near the ear and not on the cheek. Spreading caliper was placed about 2cm away from tragus by holding its tips between thumb and first finger. Then tip was slide slowly over the zygomatic arch in such a manner that the thumb touched the upper margin and the first finger the lower margin of the zygomatic bone. The joint of the caliper was lying in the mid-sagittal plane of the head.

## 6. Morphological facial index

$$\frac{\text{Morphological facial height}}{\text{Breadth of bizygomatic arch}} \times 100$$

## Observations

Data collected from the present study was subjected to statistical computation and the results have been depicted in table I and II.

Table I shows that the mean and standard deviation of total facial height in Jat Sikhs and Baniyas were  $113.52 \pm 7.21$  and  $109.95 \pm 6.08$  respectively, while mean  $\pm$  SD of bizygomatic breadth was  $137.69 \pm 4.92$  in Jat Sikhs and  $138.41 \pm 5.74$  in Baniyas. The mean and standard deviation of Facial Index was  $82.54 \pm 5.81$  and  $79.5 \pm 4.91$  in Jat Sikhs and Baniyas respectively. There is statistically highly significant difference ( $P < 0.001$ ) in the facial index of these two endogamous groups.

Different types of face shapes are shown in figure-2 Table II shows that the dominant type of face shape in Jat Sikhs was Euryprosopic (39.54%), while in Baniyas it was hypereuryprosopic (44.51%). Frequency of mesoprosopic, leptoprosopic and hyperleptoprosopic type of face is low in both Jat Sikhs and Baniyas. Mean morphological facial index of both Jat Sikhs and Baniyas fall in "Euryprosopic" type of face.

**Table 1:** Various Parameters in Jat Sikhs and Baniyas

Variable	Population	Range	Mean $\pm$ SD	p-Value
Total Facial Height (mm)	Jat Sikh Males	96.0 – 134.0	113.52 $\pm$ 7.21	d" 0.001*
	Bania Males	95.0 – 129.0	109.95 $\pm$ 6.08	
Bizygomatic Breadth (mm)	Jat Sikh Males	126.0 – 150.0	137.69 $\pm$ 4.92	e" 0.05**
	Bania Males	121.0 – 157.0	138.41 $\pm$ 5.74	
Facial Index	Jat Sikhs Males	68.0 – 98.0	82.54 $\pm$ 5.81	d" 0.001*
	Bania Males	67.1 – 91.37	79.54 $\pm$ 4.91	

Statistically highly significant \*\* Statistically insignificant

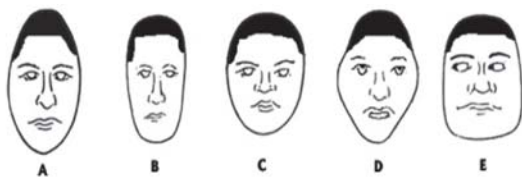
**Table 2:** Distribution of different facial parameters and index among Jat Sikhs and Baniyas

Class	Jat Sikhs	Baniyas	
Total Facial Height	Range	Percentage	Percentage -
Very low	X – 111	41.66	61.32
Low	112 – 117	32.33	28.34
Medium	118 – 123	16.67	6.99
High	124 – 129	8.56	3.34
Very High	130 – X	1.68	-
Bizygomatic Breadth	Range	Percentage	Percentage
Very Narrow	X – 127	1.99	3.33
Narrow	128 – 135	30.01	23.68
Medium	136 – 143	56.33	56.36
Broad	144 – 151	11.67	13.97
Morphological Facial Index	Range	Percentage	Percentage
Hyperleptoprosopic	X – 78.9	26.56	44.51
Euryprosopic	79 – 83.9	39.94	36.89
Mesoprosopic	84 – 87.9	16.95	15.29
Leptoprosopic	88 – 92.9	10.91	3.31
Hyperleptoprosopic	93.0 – X	5.44	-

## Discussion

Facial appearance is dependent upon soft and hard tissues of the head and face. Forensic anthropologists use the

**Figure 2:** Sketch shows the different types of face shapes – A Hyperleptoprosopic, B Leptoprosopic, C Mesoprosopic, D Euryprosopic, E Hyperleptoprosopic



relationship between the soft and hard facial tissues as a tool in establishing identification.

Anthropometry provides the operational measure for long term nutritional status. However, there are no absolute standards of size comparisons for human population, since body size has been observed to increase generation after generation [8].

There is always a need to know the normal standards of various anatomical and physiological developments. This can be done by cross sectional study which is easy and less expensive and can be applied in a country like ours [9].

Harmony and disharmony of the face depends on the relationship between individual measurements of the craniofacial complex. In an attractive face, the proportion indices are in an optimal relationship, statistically in the range of mean  $\pm$  ISD [2].

Observations of total facial height and bizygomatic breadth (table II) revealed that the highest frequency in both the endogamous groups was of very low total facial height (41.66% Jat Sikhs and 61.32% Baniyas) and medium bizygomatic breadth frequency occurred in highest percentage in both the endogamous groups (56.33% Jat Sikhs and 56.36% Baniyas).

The dominant type of face shape in Jat Sikhs was Euryprosopic (39.54%) and hyperleptoprosopic (26.56%), whereas hyperleptoprosopic (44.51%) and euryprosopic (36.89%) type of face was observed as dominant type in Baniyas, frequency of mesoprosopic face was 16.95% in Jat Sikhs and 15.29% in Baniyas followed by leptoprosopic which is 10.91% in Jat Sikhs and only 3.31% in Baniyas (Table-II).

When the results of our study was compared with the earlier reported data by Kumar et al (1990)[6] table III, the total facial height of Jat Sikhs in present study was similar, while the bizygomatic breadth (of Jat Sikhs) was more (137.69 mm) in the same endogamous group. This increase in bizygomatic breadth of Jat Sikhs can be correlated with the fact that there is a marked positive correlation between

**Table 3:** Comparison of earlier reported data with Present Study

Parameters	Present Study		Kumar et al 1990
	Jat Sikhs	Banias	Jat Sikhs
Total facial height	113.52	109.95	113.57
Brcadth of Bizygomatic arch	137.69	138.41	134.96
Morphological facial index	82.54	79.54	84.29

**Table 4:** Comparison of dominant face type in different population reported by different authors

Authors	population	gender	dominant face
Present Study	Jat Sikhs (Punjab) India	Male	Euryprosopic
	Banias (Punjab) India	Male	Hypereuryprosopic
Pandey AK 2006 <sup>[11]</sup>	Onges of Andaman and Nicobar Island (India)	Male	Hypereuryprosopic
		Female	Hypereuryprosopic
Ghosh and Malik 2007 <sup>[12]</sup>	Santhals of West Bengal (India)	Male	Euryprosopic
		Female	Hypereuryprosopic
Jahanshahi et al 2008 <sup>[13]</sup>	Fars and Turkman of Iran	Adult Male	Mesoprosopic
Golilipour et al 2003 <sup>[14]</sup>		Adult Female	Euryprosopic
Golilipour et al 2005 <sup>[15]</sup>		Newborn Male	Hypereuryprosopic
		Newborn Female	Mesoprosopic

body build and the thickness of soft tissue over zygion<sup>[10]</sup>. There is uplift in living standards, during past three decades. Moreover, previously Jat Sikhs used to put in physical labour in agriculture farming by themselves, but now the trend is of contract farming. They have started living a comparatively sedentary life. These factors may be contributing to the increased body mass index and thus increased thickness of soft tissues over zygion.

Jahanshahi et al (2008)<sup>[13]</sup> studied on northern Iran population and reported that dominant type of face shape in the Fars and Turkman males is mesoprosopic (Table-IV). So Indians Punjabis have broad face as compared to Iranian population who have globular face. They also compared the dominant face type in newborn and adults of same population <sup>[13,14,15]</sup> and concluded that from of face can change with age. Same study has also shown that gender of subject can affect the form of the face. Other authors have also reported the effect of sex on form of face. Dominant face type of onge males of Andaman and Nicobar Island of India is hypereuryprosopic <sup>[11]</sup>, while it is of euryprosopic type in Santhal males <sup>[12]</sup> of West Bengal of India (Table-IV). So from the study on different population by different authors, it can be concluded that age, gender, ethnical and geographical factors can affect the form of face.

## Conclusion

The present study shows that normally various facial types are encountered in a population so that a certain number of people have thin broad or small faces and Punjabi Banias males have a relatively broader face than Jat Sikhs males.

## Acknowledgement

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## References

1. Ternio EO: Alloplastic facial contouring by zonal Principles of skeletal anatomy. Clinics in Plastic Surgery 1992 April; 19(2): 487-510.
2. Farkas LG and Kolar JC: Anthropometric and art in the aesthetics of women's faces. Clinics in plastic surgery 1987 October; 14(4): 599-616.
3. Henneberg M, Stephan C and Simpson E: Human face in Biological anthropology: Craniometry, evolution and forensic identification. In: The Human Face: Measurement and meaning. Kluwer Academic Publishers, Netherlands 2001:1-17
4. Parwati R and Sawhney A: Midline nasal ergonomics of north Indian males. A baseline study. J Anat Soc India 1997; 46(2): 89-98.
5. Marya RK and Maini BK: A short note on the anthropometric variation in members of two communities of Haryana. Indian Anthropologist 1985; 15(2): 181-183.
6. Kumar GD, Bhowmik DC, Basu A: All India Anthropometric Survey, North Zone, Vol. 8: Punjab. Anthropological Survey of India, Calcutta; 1990: p 11 – 12.
7. Singh IR and Bhasin MK: Introduction. In: A laboratory manual on biological Anthropology, 1st edition. Kamla-Raj Enterprises, Delhi 1968; 2-3.
8. Mukerjee B and Kaul KK: Anthropometric observations on urban primary school children. Ind J Med Research 1970; 58: 1257-1271.

9. Khandiya PC, Agarwal KN and Taneja PN: Growth study in first year of life on optimal nutritional conditions. *Indian Ped Journal* 1967; 4(5): 203-207.
10. Sutton PRN: Bizygomatic diameter: The thickness of the soft tissue over the zygion. *Am. J. Phys. Anthropol.* 1969; 30:303-310.
11. Pandey A K. Cephalo-facial variation among Onges. *Anthropologist* 2006; 8(4):245-249.
12. Ghosh S, Malik SL. Sex differences in body size and shape among Santhals of West Bengal. *Anthropol* 2007; 9:143-9.
13. Jahanshahi M, Golalipour MJ, Haidari K. The effect of ethnicity on facial anthropometry in Northern Iran. *Singapore Med. J.* 2008;49(11):940-943.
14. Golalipour MJ, Haidari K, Jahanshahi M, Farahani RM. The shapes of head and face in normal male newborns in South-East of Caspian Sea (Iran-Gorgan). *J Anat Soc India* 2003; 52:28-31.
15. Golalipour MJ, Jahanshahi M, Haidari K. The variation of head and face shapes in female newborns in the South-East of the Caspian Sea (Iran-Gorgan). *Eur J Anat* 2005; 9:95.

# Reterospective analysis of complications of cesarean section in rural western U.P.

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## Abstract

## Background

Cesarean section(CS) is the most commonly performed obstetric surgical procedure throughout the world. Usually this is a life saving procedure for both mother as well as new born baby, but it also have some complications, related to both surgical and anaesthetical.

## Aims & objectives

To evaluate different complications encountered during and after cesarean section within a period of 10 years at LSRH & SIMS and its management.

## Materials & methods

An analysis of 8550 patients was done at LSRH & SIMS during 2000-2009. The patients who underwent cesarean section whether it was elective or emergency, cases booked or unbooked, done for various indications constituted the subject of study. The patients were analysed with respect to types of maternal morbidity encountered.

## Results

In our study, we analysed 8550 deliveries during 2000 to2009, out of which 22% of patients were subjected for CS. Out of 22% of CS, 86.6% patients were operated as emergency and 13.3% as elective section. In present study, minor & major morbidity were seen in 33.3% of cases. Rest of the patients recovered without any problem in postoperative period.

## Conclusion

In present study, incidence of CS was 22%. Most common indication for CS was foetal distress, followed by previous CS, prolonged labour, malpresentation & APH, etc. Incidence of maternal morbidity in this study was 33.3 %.

## Key word

Cesarean section, un-booked, fetal distress.

## Introduction

Cesarean delivery is defined as birth of a foetus through incision in abdominal and uterine wall after the age of

viability. Incidence of CS increased gradually from 5.2% in 1970-72 to 10.1% in 1982-84 (Confidential enquiry in England and Wales 1970-72, 1980-84), might be due to increase in the availability of investigation facility even. Most commonly employed method of CS is lower segment CS.

Most common indications are cephalo- pelvic disproportion, previous CS, foetal distress, malpresentation, etc. Complications of CS are many and they are related either to surgery or type of CS done and anaesthetic complications. Most important and dangerous complication of CS is haemorrhage. It may be primary, delayed primary or secondary.

In cases of previous CS, there is risk of injury to bowel or bladder as these might be adherent. Incidence of wound infection is 1-9% (Rehu & Nielson, 1980). Patients might present in follow up with incisional hernia particularly with longitudinal incision.

## Material and method

This study carried out in department of Obstetrics & Gynaecology at SIMS & LSRH. Both emergency and elective CS was included in this study. Detailed history, clinical and obstetrical examinations were analysed. The different types of anaesthesia, different approach to CS and its complications were analysed.

## Results

In this study 8550 cases of deliveries were analysed during 2000-2009 at SRH & SIMS. Incidence of CS was 22% in our study. Majority (6241) belonged to unbooked category and 2309 cases were booked. Patients interfered belonged to age group 21-35 yrs. In cases studied, 86.6% were emergency and 13.3% were elective CS. Of 1881 cases of CS undertaken in present study, minor and major morbidity were seen in 33.3% of cases. Rest of the patients recovered without any problem in post- operative period. Most common indications of CS were foetal distress, followed by previous CS, prolonged labour, malpresentation & APH, etc.

Incidence of morbidity was high in the series because 86.6% of CS were performed as emergency procedure and 73.3% cases were not taken any ante natal checkup. Majority of our patients belonged to low socio- economic status having poor hygiene. Majority of patients had tried the normal vaginal deliveries in home by some untrained

dais. These patients were susceptible to develop complications in post-operative period. Most common complication following CS was PPH (40%) whether it was intrapartum, or immediate post partum or delayed PPH. Next common complication was wound infection (35%) - other complication encountered were UTI (5%), anaesthetic complications (10.15%), chest infection (5%), etc. The reported complications are injury to bladder & viscera which I did not encounter in my study. In this study, we encountered three maternal mortalities two of which were due to severe PPH. One case of severe eclampsia expired due to severe neurological deficit despite all resuscitative measures.

## Discussion

CS has become a very common operation due to various investigative procedures for foetal surveillance to detect high risk pregnancies at earliest. CS is an extremely safe operation. It has improved foetal survival, as compared to deliveries forceps or vaginal. Most of serious complications associated with CS are not due to operation itself.

**Table 1:** Comparative

	Year	incidence%
Taylor et al	1992	17.5
Taffel et al[9]	1988	25
Notzon et al [7]	1987	17
Present study		22

The high incidence of 22% in this study may be attributed to large number of cases being handled outside the hospital by dais or being complicated due to high risk factors. Incidence of CS was high in primigravida (33%) because of in-coordinate uterine action leading to labour dystocia, cephalo pelvic disproportion and foetal distress. The next group was of second gravida patients with indication of repeat CS (30%). Multi para patients are more prone to have APH, malpresentation and obstructed labour.

Indication	No. of cases	Incidence
Foetal distress	470	25
Repeat CS	413	22
Prolonged labour	339	18
Obstructed labour	302	16
Malpresentation	151	08
APH	113	06
PIH	075	04
Bad obstetric history	018	01

Most common indication for CS in this study was foetal distress (25%) which tallies with figures of and S. Jain et al (1985- 86) [4].

In present study, foetal distress was diagnosed by abnormalities of foetal heart sound by simple auscultatory method and meconium stained liquor. In other studies, high incidence of CS for foetal distress was due to earlier

detection by electronic foetal heart monitoring. Next common indication for abdominal surgery in present words was repeat CS (22%). M.A. Deshmukh et al (1980) and Wadia of Bombay (1987) reported 19.05% and 24.2% of cases respectively for respect CS. With proper supervision, it is possible to deliver up to 64% of previous cesarean vaginally (Menon 1963, China et al 1989).

Out of 1881 cases of CS undertaken in present study, minor and major morbidity was seen in 33 % of cases. Incidence of morbidity was high in this series because 86.6% of CS was done as emergency procedure and 73.3% cases were unbooked. Majority of our patients belonged to low socio-economic status (50%) having no knowledge of hygiene at all.

## Types of maternal morbidity in cases of CS chart

Most common complication following CS was PPH whether it was intrapartum, immediate postpartum or delayed PPH. Bleeding on placental site was controlled by exploring uterus for any retained bits of placenta, manual message of uterus, added by injection ergometrine and oxytocin infusion and in some case prostodine injection. In one case, sutures of 8 were taken at placental site to control haemorrhage. In another case, subtotal hysterectomy had to be performed when bleeding was not controlled in spite of all above measures.

In 10 cases, there was difficulty in delivery of baby. Incision extended laterally into vessels and there was severe intrapartum haemorrhage. A rapid first line of intensive sutures was placed to close uterine incision.

PPH occurred in 20 patients within twenty four hours. It was managed conservatively.

Secondary PPH was seen in 20 patients. All cases were managed conservatively. Blood transfusion was given in all patients with PPH after blood grouping and cross matching.

In this series, 35% patients suffered from wound infection, 4% patients had wound dehiscence and are patients landed into burst abdomen.

Wound infections were treated with broad spectrum antibiotics and drainage and drainage of pus. In cases of wound dehiscence, secondary tension sutures were taken after wound debridment. In case of burst abdomen, patient was given IV fluid antibiotics and blood transfusion, separtory was undertaken and secondary tension sutures were given.

Two hundred forty-five women with at least two cm. of subcutaneous fat were randomized to closure of the camper fascia or no closure with cesarean delivery Naumann RW et al (1995)[6]. There was a significant difference in the incidence of wound disruption from all causes between the two groups: 14.5% in subcutaneous closure groups compared with 26.6% when the subcutaneous tissues were not reapproximated. Within a period of fifteen months in Alabama, Parker KM et al (1995)

[8] presented two cases of fatal post cesarean endometritis. Study done by Donowitz L G et al in 1986 [2] describes the incidence of endometritis following CS in different patient groups at university of Virginia during one year period.

In this study, UTI occurred in 5% cases. Buchholz NP et al (1994) [1] analysed 1438 deliveries by CS with regard to urological complications and urinary tract injuries.

5% patients had paralytic ileus. Four cases of Ogilvie's syndrome (Acute colonic pseudo obstruction) are reported by Hamed AD (1992) [3]. They were managed conservatively. A case of omental abscess following LSCS is reported by Williams BT (1979) [10].

10% patients suffered from post spinal headache and 0.15% patients developed aspiration pneumonia. There was accidental cystotomy in one case while separating the bladder from the uterus as it was adherent due to previous CS. Bladder was repaired immediately in two layers. One patient developed vesico- vaginal fistula on 15<sup>th</sup> post operative day. She was repaired after six months.

In our study, 3 patients expired, two of which were due to severe PPH that did not respond to any of conservative measures and patients. One case of severe eclampsia expired due to severe neurological deficit despite all resuscitative measures.

McIndoe AK et al (1995) [5] have described a previously asymptomatic patient who presented with cardiac arrest at induction of general anaesthesia for emergency CS and subsequently developed acute cardiac failure.

## Summary and conclusion

Incidence of CS was 22% in present study at SRH & SIMS. Incidence of maternal morbidity in this study was 33.3%. Incidence of morbidity was high because 86.6% of CS was performed as emergency procedure and 73.3% of cases were unbooked. Most common complication following CS was PPH followed by wound infection.

## References

1. Buchholz NP, Daly- Gradeau E, Huber- Buchholz MM. Eur J Obs Reprod Biol; 1994 56(3):161-3
2. Donowitz LG, Norris SM. Infect Control; 1985: 6(5):189-93
3. Hamed AD, Dare Fo Int J Gyn & Obs; 1992:37(1):47-50
4. Jain S., S. Gupta. Ind. J Gyn & Obs; 1988:38, 3:261
5. MC Indoe AK, Hammond EJ, Babington PC. Br J Anaesth; 1985:75 (1): 97-101
6. Naumann Rww, Hauth JC, Owen J, Hodgkins Pm, Lincton T Obs. & Gyn; 1995:5(3):412-6
7. Notzon F.C, Coles, Rev. F.R. Gyn & Obs; 1985: 86(7-9) 503-10
8. Parker Km & Embry JH. Ala Med ; 1995:64(10):13-6
9. Taffel S.M. Am. J. Public Health; 1987: 77, 955- 9
10. Williams BT. South Med J; 1979: 72(8):1025-6

# Implant considerations in children and adolescent patients

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## Abstract

There are some congenital disorders which can lead to absence of teeth in children. Such children require replacement of teeth for functional and psychological reasons. As the growth of the jaws is still incomplete, it was generally accepted that removable partial denture is the treatment of choice in children.

Various authors have debated the pros and cons of placing implants in children and adolescent patients. All are of the opinion that an understanding of dental development and cranio facial growth is a must for anyone trying implants in children. Hence, an understanding of the direction of growth of the jaws, the problems of placing implants and the importance of vigilant recare programme in children is a necessity before attempting implants in children.

## Key words

Growth, Implants, Children, Adolescence, Implant supported prosthesis.

## Introduction

The reasons for missing teeth in children's include congenital disorders, pathology, trauma and others. Prosthodontic rehabilitation is required in such children depending on the individual status of the existing dentition, the functional status of mastication, phonetics, esthetic aspects and psychological well being. The replacement of missing teeth in children differs from that of adults and there are some important factors to be considered in treatment planning.

The factors include,

**Growth:** Jaw growth in children is continuous till 18 to 22 years and the presence of teeth is vital for the development of anatomy and physiology in the adjacent structures. Any interim prosthesis should not interfere with the growth of these structures.

**Space management:** There is a need for space management to facilitate proper eruption of permanent

teeth. The clasps and the temporary denture base should not interfere with the eruption of natural teeth.

**Neuromuscular skills:** The neuromuscular skills in child are not as developed as that of adult. The better the neuromuscular coordination, the better is the adaptation to the temporary denture.

**Patient and parent management:** The child patient must understand the need for the prosthetic replacement; its maintenance and the importance of good oral hygiene. The child's cooperation needs to be gained through behavioral management. The parents' attitude, motivation and understanding of the proposed treatment and its limitations need to be carefully evaluated before any treatment is rendered.

**Modification in the procedures:** The modification of existing teeth for their preservation and maximum support, alteration of the techniques in fabrication of prosthesis and the modification and/or replacement of the prostheses is to be kept in mind during child rehabilitation. Numerous treatment options for edentulous space in children and adolescence include; removable prostheses and recently the dental implants. Removable prosthesis which includes removable partial dentures, complete dentures and overdentures are often the treatment of choice to replace missing teeth and/or restore vertical dimension of occlusion prior to definitive treatment. The advantages of overdentures in cases of hypodontia are well documented. Removable prostheses are easily modified or remade during the growth period offering an easy, affordable, and reversible method of dental rehabilitation. Fixed Prosthodontic treatment is seldom used even as an interim prosthesis in the treatment of hypodontia. Fixed partial dentures with rigid connectors should be avoided in young, actively growing patients as it may interfere with jaw growth.

The successful use of implants in adults has aroused the interest of the clinicians to try them in younger patients. There is no doubt that the children who have congenital anomalies can benefit remarkably from an implant supported oral rehabilitation carried out in childhood.<sup>1</sup> However, dental and skeletal growth is a major compounding variable related to the use of dental implants in adolescent patients.<sup>2</sup> Clinicians should have an understanding of the potential risks involved in placing implants in jaws that are still growing and developing and consider the effect that implants have on craniofacial growth.<sup>3</sup>

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For a stable implant position, it is generally recommended to wait for the completion of dental and skeletal growth. In a growing child, the growth and development of maxilla and mandible are different as are those in the specific areas of each arch.<sup>4-7</sup> Transversal skeletal or alveolar dental changes are less dramatic in mandible than maxilla.<sup>8</sup> However if implants are to be placed in children or adolescents, the two primary concerns are the effect of growth on the long term relative position of the implant and the effect of implant supported prosthesis on future dental and skeletal growth.<sup>2</sup>

Normally the early growth in maxilla is due to growth of the cranial base and the later growth is extremely variable and can be vertical, transverse and antero posterior. Transverse growth occurs at the midpalatal suture and implant prosthesis crossing the suture will restrict growth. In the mandible, the growth in the posterior region occurs predominantly in late childhood with large amounts of anteroposterior, transverse and vertical growth apart from rotational growth [Downward and forward, mediated by oppositional condylar growth]. Where as in anterior mandible, there is minimal alveolar growth when teeth are missing due to early stabilization of the mandibular symphysis. Major transverse growth is complete in early childhood. It is the most suitable site for implant placement. Placing implants in this region also will diminish the residual alveolar resorption.

In the absence of maxillary teeth, the alveolar ridges will not develop, and the maxilla will be underdeveloped both sagittally and vertically. In contrast, Mandibular growth is not dependent on the presence of teeth. Therefore, in the presence of hypodontia or anodontia, the relationship between the two jaws will tend to be disproportionate with class III development as growth continues throughout the normal growth period<sup>9</sup>.

## Discussion

Anodontia is a genetic disorder defined as the absence of all teeth and is extremely rarely encountered in a pure form without being part of a syndrome. Rare but more common than anodontia are hypodontia and oligodontia. Hypodontia is genetic in origin and usually involves the absence of 1 to 6 teeth. Oligodontia is genetic as well and is the term most commonly used to describe conditions in which more than six teeth are missing. These conditions may involve the primary or permanent sets of teeth, but most cases involve the permanent teeth.

One of the commonest causes of congenitally missing teeth in children reported in the literature is due to ectodermal dysplasia (ED). Young children with ED and anodontia in the mandible, present special challenges while placing implants.<sup>10</sup> Implant survival rates vary between 88.5% and 97.6% in patients with ED and between 90% and 100% in patients with tooth agenesis. Implants placed in adolescent ED patients do not have a significant effect on craniofacial growth, while implants placed in ED patients younger than 18 years have a higher

risk of failure<sup>11</sup>. The main risk factors could be the small jaw size, the pre-operative condition, lack of patient monitoring following surgery and orofacial motor dysfunction, rather than the ED itself.<sup>10,11</sup> Some of the authors have argued that endosseous implants can be successfully placed and can provide support for prosthetic restoration in patients with ectodermal dysplasia.<sup>12</sup> Studies have shown that these patients benefit remarkably from an implant supported oral rehabilitation<sup>13</sup> particularly because children do not use removable partial dentures. The loaded implants help to ensure maintenance of ridge height, prevent supra eruption, and maintain stable occlusion.

Although the development of techniques for osseointegrated implants offer new possibilities for the prosthodontic rehabilitation of such children, it was concluded that implant surgery in small children must not be considered routine treatment.<sup>14</sup> It is recommended to wait for the completion of dental and skeletal growth except for severe cases of ectodermal dysplasia.<sup>15</sup> It is accepted by most of the authors that the safest time to place implant in such children seems to be during the decline of adolescent growth curve determined by cephalometric radiographs, serial measure of stature or hand-wrist radiograph.<sup>8</sup>

## Problems and precautions

Implants in the maxilla can behave like ankylosed tooth<sup>16</sup>, cannot participate in growth resulting in growth disturbances, unpredictable implant dislocations in vertical and antero posterior direction and even implant losses due to resorptive aspects of growth at the nasal floor and anterior surface of maxilla. It is concluded that insertion of implant in growing maxilla should be avoided until early adulthood.<sup>8</sup>

In the posterior mandible, implants may become submerged resulting in both functional and esthetic disadvantages later like infra occlusion and multidimensional dislocation when compared with the developing teeth. As a result there are no reported implant insertions in the posterior mandible.<sup>8</sup>

Overall, implants in any region can interfere with the position and eruption of adjacent tooth germs. There may be morphological changes due to trauma to tooth germs and disorders of eruption. Osseointegration may be lost as the growth takes place. In order to avoid these problems, some clinicians have tried placing implants buccally with success. Implants placed after 15 years in girls and 18 years in boys or when two annual cephalograms show no change in the position of the adjacent teeth and alveolus are said to have the most predictable prognosis.<sup>6,9</sup>

If a decision is made of implant placement, it is advisable to restore larger edentulous areas with implants than to place a single implant supported crown.<sup>1,16,17</sup> Considering the anatomical and morphological features in pediatric patients mini and micro implants are being introduced.<sup>8</sup> A combination of well executed Implant-supported/tooth-

supported, overdenture (hybrid) prosthesis would be an excellent choice in rehabilitation of congenital subtotal anodontia later in life in contemporary dental practice<sup>18</sup>. However, the decision for implant placement is based not only on growth, but also the number and location of the missing teeth. In patients who present with complete anodontia, implants can be planned in the maxilla and anterior mandible as early as age 7. These may be classified under provisional implants. It has to be kept in mind that surgery [segmental osteotomy or distraction osteogenesis] may be necessary once growth is complete to reposition of the implant segment to a more favorable position thereby to correct the jaw size discrepancy. Implants may have to be replaced<sup>7</sup> or the implant prosthesis may have to be modified or remade over time by utilizing pink porcelain or acrylic resins for fixed or removable implant supported prosthesis<sup>9</sup>.

Some studies have shown excellent long term results achieved after appropriate case selection, careful handling of the soft and hard tissues and good occlusal harmony. But usually a common problem faced in case of missing teeth is lack of sufficient bone for implant placement and this may be due to local to general decrease of growth stimuli of the jaw due to absence of large numbers of teeth.

## Conclusion

Ideally the implants are placed once the skeletal growth is completed, but in cases of partial or complete anodontia the use of implants is becoming popular. Placing implants in a child patient should be a team effort consisting of surgeon, pedodontist, prosthodontist, orthodontist and periodontist. There is no doubt that implants would greatly assist in prosthesis support. The clinician should understand the disadvantages of early placement and weigh those factors against esthetic and functional advantages afforded by implants.

Patients with implant assisted restorations should be evaluated frequently to ensure the health of the implant and its surrounding tissue as well as to assess the effect of the prosthesis on the overall growth and development of the jaws. An extremely vigilant care programme is necessary.

## References

- Guckes AD et al. Using endosseous dental implants for patients with ectodermal dysplasia. *J Am Dent Assoc* 1991;122:59-62.
- McDonald. Prosthodontic treatment of the adolescent patient. In, *Dentistry for the child and adolescent*, 8<sup>th</sup> edition. New Delhi, Mosby publishers, 2004;504-523.
- Brahim JS. Dental implants in children. *Oral Maxillofac Surg Clin North Am* 2005;17:375-381.
- Bjork A, Skieller V. Growth of the maxilla in three dimensions as revealed radiographically by the implant method. *Br J Orthod* 1977;4:53-64.
- Cronin RJ, Oesterle LJ. Implant use in growing patients: treatment planning concerns. *Dent Clin North Am* 1998;42(1):1-34.
- Cronin RJ, Oesterle LJ, Ranley DM. Mandibular implants and the growing patient. *Int J Oral Maxillofac Implants* 1994;9:55-62.
- Oesterle LJ, Cronin RJ, Ranley DM. Maxillary implants and the growing patient. *Int J Oral Maxillofac Implants* 1993;8:377-387.
- Shobha Tandon. *Pediatric Prosthodontics*. In, *Text book of Pedodontics*, 1<sup>st</sup> edition, Hyderabad, India, Paras Medical publishers, 2003;601-613.
- Sharma AB, Vargervik K. Using implants for the growing child. *J Calif Dent Assoc* 2006 Sep;34(9):719-24.
- Bergendal B, Ekman A, Nilsson P. Implant failure in young children with ectodermal dysplasia: a retrospective evaluation of use and outcome of dental implant treatment in children in Sweden. *Int J Oral Maxillofac Implants* 2008 May-Jun;23(3):520-4.
- Yap AK, Klineberg I. Dental implants in patients with ectodermal dysplasia and tooth agenesis: a critical review of the literature. *Int J Prosthodont* 2009 May-Jun;22(3):268-76.
- Kearns G, Sharman, Perrot D. Placement of endosseous implants in children and adolescents with hereditary ectodermal dysplasia. *Oral surg Oral med Oral Pathol Oral radiol Endod* 1999;88:5-10.
- Sweeney et al. Treatment outcomes for adolescent ectodermal dysplasia patients treated with dental implants. *Int J Paediatr Dent* 2005;15:241-248.
- Bergendal T, Ederdal, Koch. Osseointegrated implants in the oral rehabilitation of a boy with ectodermal dysplasia. *Int Dent J* 1991;41:149-156.
- Percinoto C et al. Use of dental implants in children: A literature review. *Quintessence Int* 2001;32:381-3.
- Westwood RM, Duncan JM. Implants in adolescents: a literature review and case reports. *Int J Oral Maxillofac Implants* 1996;11:750-755.
- Ledermann PD, Hassell TM, Hefti AF. Osseointegrated dental implants as alternative therapy to bridge construction or orthodontics in young patients: seven years of clinical experience. *Pediatr Dent* 1993;15:327-333.
- Dhiman R, Singh P, Roy Chowdhury SK, Singla NK. Complete mouth rehabilitation of sub total congenital anodontia with indigenous implant supported prosthesis. *J Indian Prosthodont Soc* 2006;6:90-94.

# Incidence, correlates and outcomes of Low Birth Weight – A one year longitudinal study

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## Abstract

## Background

Birth weight is a reliable and sensitive predictor of a newborn's chances for survival, growth and long term physical and psychosocial development. Thus knowing the magnitude and associated risk factors of low birth weight (LBW) will help in minimizing its incidence in the community.

## Aims

To find out the incidence of LBW babies, its risk factors and its effects during the first year of life.

## Study design

This longitudinal study was done in three subcentre areas of South India.

## Subjects

All the 194 babies born from November 2004 to April 2005 formed the birth cohort.

## Outcome measures

Weight of the newborn was recorded in the initial visit followed by monthly follow up visits to enquire about their morbidities.

## Results

The incidence of LBW among 194 babies was 2.48 per 1000 live births. The risk factors significantly associated with LBW were age at first pregnancy below 19 years, less than 100 or no intake of iron and folic acid tablets (IFA) during antenatal period, birth spacing of less than 2 years between pregnancies and babies of Scheduled caste or tribe (SC/ST) families. Incidence of episodes of all morbidities was more and that of anemia was significantly more among LBW compared to normal birth weight babies during the first year of life.

## Conclusions

LBW was affected by multiple risk factors with consequent effect on occurrence of morbidities. Such factors need to

be affectively controlled to improve child health and development.

## Keywords

Low birth weight, Incidence, Correlates, Outcomes, Morbidities, Community, Longitudinal study.

## Introduction

Birth weight is a reliable and sensitive predictor of a newborn's chances for survival, growth and long term physical and psychosocial development.<sup>1</sup> Babies with low birth weight (LBW) are at a greater risk of dying during infancy. There is also a significant risk of increased morbidities and developmental problems during childhood associated with it. At the family level, the cycle of poor nutrition perpetuates itself across generations. LBW girls, in the absence of positive intervention to break the cycle, grow poorly, become stunted women and are more likely to give birth to LBW babies.<sup>1</sup> LBW is thus a good indicator of mother's nutritional status. Prevalence of LBW in a country is a good summary measure reflecting its public health problems and has been a very sensitive public health indicator for all the developing countries including India. In India over 30% of newborns are estimated to be of LBW.<sup>2</sup> Recognizing the importance of birth weight measurement, the 34<sup>th</sup> World Health Assembly in 1981 included it as one of the global indicators for monitoring of health of the community.<sup>3</sup> Birth weight is routinely measured and recorded in babies delivered at health institutions. In most of the developing countries, majority of newborns are delivered at home and are unlikely to be weighed.<sup>4</sup> Available data on magnitude as well as risk factors of LBW from different parts of the world are based on institutional deliveries and thus cannot be considered representative of the large population born at home. There is a need of conducting community based studies to find risk factors of LBW. With this background a longitudinal community based prospective study was undertaken to find out the incidence of LBW babies, to find out its association with socio demographic and obstetric factors and its effects during the first year of life.

## Methods

A longitudinal study was conducted on a birth cohort of

194 infants who were followed up for a period of one year. It was carried out in the field practice area, Kinaye of Jawaharlal Nehru Medical College in Belgaum District of Karnataka State, in South India.

Kinaye has a primary health centre with five subcentres under it, of which three were randomly selected for the study namely Santibastwad, Machhe and Peeranwadi. 'Subcentre' is the peripheral most outpost of health delivery in India and each one caters for approximately 5000 population. Study period was from November 2004 to April 2006. All children born from November

2004 to April 2005 formed the birth cohort that was followed up. During the initial phase, the investigator visited houses of mothers within 10 days of childbirth for measuring and recording birth weights. After taking consent from the mother, weight of baby was recorded using a portable beam type of weighing machine. In case of babies delivered in health facilities birth weight was collected from available documents /certificates. Base line data pertaining to socio demographic profile, antenatal care, chewing habits etc of the mothers were also recorded on a pretested proforma. Thereafter monthly follow up visits were done for one year (till the completion of infancy) to enquire about their morbidities which was followed by a detailed clinical examination. Document verification was done in case child had illness in between the visits.

**Inclusion Criteria:** All newborns of mothers who were permanent residents of the study area and who were available for follow-up for one year and singleton pregnancies. **Exclusion Criteria:** Babies born to mothers who had come to parental house for delivery.

It is a common cultural practice in India for pregnant women to come to their parental house few months before delivery and stay there till few months after. This is to obtain better care and support during these vital periods. When the baby is few months old, they go back to their place of residence. That would make them unavailable for a full year of follow up.

Data analysis was calculated in rates and proportions using SPSS Inc. Illinois, USA version 10.0. Socio economic status was calculated using Modified B G Prasad's classification of 2004.<sup>5</sup>

## Results

Of the total 194 deliveries, 49(25.3%) took place at home, 67(34.5%) at government health centres or hospitals and 78(40.2%) at private hospitals. Majority of postnatal mothers 169 (87.1%) were between 19-29 years, were literates 137(70.6%) and were of poor socio economic class IV 92(47.4%) & V 82(42.3%). Consanguineous marriage was seen among 60(30.9%)

mothers and 78(40.2%) of them were married below the age of 18 years. Also 82(42.3%) of the mothers were below the age of 19 years when they were pregnant for the first time.

Out of the total 194 babies, majority 104(53.6%) were females.

Mean and standard deviation of birth weight of the newborns was 2.64±0.47 Kg and it was 2.68 ±0.43Kg for males and 2.60±0.38 Kg for female babies respectively.

A total of 48(24.8%) newborns were of low birth weight. Proportion of LBW babies were slightly more among males 23(25.6%) compared to females 25(24%). (Table 1)

Greater proportion of LBW babies were of illiterate mothers (31.6%) compared to that of literate mothers (21.9%). The proportion of LBW babies among the poorest socio economic status families (Class V) was 29.3% compared to 21.4% among the rest.

LBW were seen significantly more 22(34.9%) in families of

**Table 1:** Gender wise distribution of infants according to birth weight.

Birth weight (Kg)	Males		Females		Total	
	No.	%	No.	%	No.	%
1.5-2.0	1	1.1	4	3.8	5	2.6
2.0-2.5	22	24.4	21	20.2	43	22.2
2.5-3.0	51	56.7	71	68.3	122	62.8
3.0-3.5	14	15.6	6	5.8	20	10.3
3.5-4.0	2	2.2	2	1.9	4	2.1
Total	90	100.0	104	100.0	194	100.0

$\chi^2=7.33$ , DF=4, P=0.119

Scheduled caste and tribe families (backward castes in India) compared to 26(19.8%) among others. ( $\div 2= 4.76$ , P=0.029)

Percentage of LBW with respect to age at first pregnancy (among 50 primiparous mothers) was significantly more in less than 19 years age group 7(58.3%) compared to other age groups 6(15.8%). ( $\div 2= 8.579$ , P=0.003)

The relative risk was found to 3.69 times more in the former than the latter.

LBW was seen more common among consanguineous marriages 18(30%) compared to non consanguineous marriages 30(22.4%). Proportion of LBW babies were more in working mother 14(35%) compared to house wives 34(22.1%). Out of 13 mothers with history of preeclampsia or eclampsia during their antenatal period, 5(38.5%) gave birth to LBW babies compared to 43(23.8%) among the rest.

The proportion of LBW babies was slightly higher among mothers with less than 3 antenatal care visits (ANC) visits 10(27.8%) compared to those with 3 or more ANC visits 38(24.1%).

In the present study it was found that percentage of newborns with low birth weight significantly decreased with increased intake Iron and Folic Acid (IFA) tablets during antenatal period ( $c^2=4.36$ , DF=1, P=0.037). (Table

2)

Proportions of LBW babies were more among mothers who were habituated to chewing tobacco 6(35.3%) as compared to those who were not 42(23.7%).

LBW was seen more among preterm babies 4(40%) compared to normal or post term babies 44(23.9%). The percentage of LBW with respect to birth order 1, 2, 3 was

**Table 2:** Association between birth weight of newborns and Iron & Folic acid tablets (IFA) supplementation during mother's antenatal period.

IFA Supple mentation	LBW babies	NBW babies	Total
Not taken	7 (38.9%)	11(64.7%)	18(100%)
<100 tablets	20(30.3%)	46(69.7%)	66(100%)
≥100 tablets	21(19.1%)	89(80.9%)	110(100%)
Total	48	146	194

$\chi^2=4.36$ , DF=1, P=0.037

found to be 13(26%), 21(23.3%), 15(38.5%) respectively. Among 144 multiparous mothers, LBW was seen significantly more among mothers having birth interval of less than 2 years 20(39.2%) compared to when it was more than 2 years 15(16.1%). ( $\div 2=9.54$ , P= 0.002)

Risk factors like parity of mothers, history of birth asphyxia, congenital anomalies in new born, type of family and paternal tobacco smoking or chewing habits were seen more among normal birth weight (NBW) babies than LBW babies.

In the present study, the incidence of morbidity episodes (Respiratory tract infections, Diarrhoea, Skin diseases, Otitis media, Anaemia, Vitamin A deficiency, Eye Infections etc) in first year of life was found to be slightly higher among infants with low than normal birth weight. (Table 3)

It was observed that 24 (50%) infants with LBW were anemic and they developed 31 episodes of anemia at the end of 1 year at an incidence rate of 0.65/infant/year. 42(28.8%) infants with NBW were anemic and they developed 48 episodes of anemia till the end of 1 year at an incidence rate of 0.33/infant/year. This difference in

**Table 3:** Association between birth weight of infants and incidence of morbidity disorders.

Birth Weight	No. of infants	Total episodes of morbidities till the end of one year	Incidence per infant per year
LBW	48	161	3.35
NBW	146	475	3.25
Total	194	636	3.28

$\chi^2=0.109$ , DF=1, P=0.741

episodes of anemia was found to be statistically significant ( $\chi^2=9.004$ , DF=1, P=0.002). (Table 4)

Delayed milestones during infancy were seen in 16(33.3%) babies with LBW compared to 45(30.8%) babies of NBW. ( $\chi^2=0.106$ , P=0.745)

Out of 4 babies with malnourishment at the end of infancy,

3 were of LBW.

**Table 4:** Association between LBW and anaemia in infants.

Birth weight	Infants with anaemia	Infants without anaemia	Total
LBW	24(50%)	24(50%)	48(100%)
NBW	42(28.8%)	104(71.2%)	146(100%)
Total	66	128	194

$\chi^2=25.846$ , DF=1, P=0.000

## Discussion

Birth weight is an important predictor of neonatal survival and thus has long been the subject of clinical and epidemiological investigations. The magnitude of LBW is a sensitive indicator of public health of a community. The incidence of LBW in our study was found to be lesser than incidence of LBW observed by other Indian studies such as by Mondal (28.5%)<sup>6</sup>, Hirve et al (29%)<sup>7</sup> and Biswas et al (31.3%).<sup>1</sup> Such occurrence of LBW differentials among different population groups of same race might be due to ethnic/genetic factors or due to varying time frame when these studies were done.<sup>8</sup>

In a number of previous studies including the present one it was observed that mother's age at pregnancy was significantly associated with LBW.<sup>(7, 9-12)</sup> This is because mothers below 20 years at the time of pregnancy might have reproductive and anatomical immaturity. Similarly, physical exhaustion could be the reason behind deliveries within 2 years of birth of the previous child significantly resulting in LBW babies as observed in other studies.<sup>(11, 13, 14)</sup>

The present results are in agreement with some of the previous works<sup>(7, 10, 15)</sup> that poor economic condition increases the risk of delivering a LBW baby. This is because poor mothers suffer from nutritional deficits resulting in poor weight gain during pregnancy resulting in LBW babies. This could also explain the significant association of LBW babies found more among mothers of Scheduled caste and Schedule tribe families in our study. However as the present study lacks information on participant mother's nutritional profile we cannot further substantiate our inferences.

Mother's education might affect birth weight indirectly as better informed they are, better will be their level of antenatal care, nutrition and spacing between births. This could be the reason behind greater number of LBW babies of illiterate mothers than of literate mothers in our study similar to observations of previous studies.<sup>(1, 10, 11, 15, 16)</sup>

Mother's with history of consanguinity were also found to give birth to more number of LBW babies. Though not a significant association, it gives hint towards genetic factors involved in etiology of LBW babies.

Another important observation was LBW babies being more common among working mothers. This was similar to the observations of Vietnam study<sup>17</sup> were farming

mothers and Thailand study<sup>11</sup> were agricultural labourers doing hard physical work or having to walk more than 2 hours to their work place giving birth to more number of LBW babies.

The proportion of LBW babies were more among mothers with fewer numbers of antenatal visits as observed in ours and other's studies.<sup>(1, 9, 11, 13, 14, 16-20)</sup> Infrequent antenatal visits (less than 3) will deny mother of periodic obstetric examination and advices on good antenatal care and low cost nutritious foods. Also in this study LBW was significantly more among mothers who did not take or took less than 100 IFA tablets during pregnancy. This emphasizes the additional benefit of IFA tablets in improving the birth weight of newborns hence should be prophylactically taken by all pregnant mothers for the required number of days.

LBW babies seen more among tobacco chewing mothers in our study is due to the vasoconstrictor influence of nicotine causing placental insufficiency.<sup>21</sup> This association was however not significant, probably because exposure risk to tobacco is lesser when it is chewed than smoked. Significant association in smoking mothers giving birth to LBW babies was observed in studies done in other parts of the world.<sup>(11, 13, 15, 20)</sup>

LBW babies were seen more among mother's with positive history of pre eclampsia and eclampsia during gestational period. Other studies too have shown a significant association of toxemia with LBW.<sup>(11, 16)</sup>

LBW being found among a greater proportion of preterm babies in this study has been supported by other studies where significant association was seen.<sup>(7, 13, 16, 22)</sup>

Repeated births are known to deplete maternal nutrition and stores of iron. This could be the reason why LBW was seen more commonly among babies of birth order 3 and above. Similar observations were made in other studies where LBW frequency was most from birth order 4 and beyond.<sup>(6, 11, 20)</sup> Greater proportion of LBW babies among birth order 1 than 2 in our study could possibly be due to, more than half of LBW babies in the former category belonging to mothers aged below 19 years at the time of delivery.

In our study the incidence of morbidity episodes during first year was higher among LBW infants compared to NBW infants. This was similar to the observations of a study done in rural Malawi.<sup>23</sup> In another study done in Egypt it was found that infants with LBW had episodes of respiratory tract infections for a longer duration.<sup>24</sup> This means that LBW status increases the susceptibility towards infections.

The percentage of infants with anaemia and incidence of anaemic episodes till the end of infancy was significantly more among LBW babies than NBW babies in our study. This was comparable to the observations made in another study done in Thailand.<sup>25</sup> The significant association of LBW and susceptibility of anaemia during infancy should alert the mothers to feed their LBW babies with more of iron rich foods during weaning period and if required iron supplements additionally. The proportion of LBW babies

being more among infants who became malnourished by the end of infancy again stresses the importance of additional nutritional care required for LBW infants.

LBW status has also seen to influence the mental development as proportion of delayed milestones was seen more among LBW babies than NBW infants.

## Conclusion

The incidence of LBW was found to be 2.48 per 1000 live births. The significant risk factors for LBW observed were age at pregnancy below 19 years, birth spacing of less than 2 years, babies belonging to SC/ST families and IFA supplementation of less than 100 tablets during antenatal period. With respect to the outcomes of LBW, greater morbidity episodes in first year of life were noted when compared with that of NBW infants. This was significant with respect to anemia. Therefore LBW has long lasting effects on future health being of children. Understanding the extent of LBW and its risk factors will help in formulating an effective maternal and child health care programme. The health professionals should then target limited resources for improving maternal education and nutritional status. They should provide wider availability of contraception and make sure that mother at greatest risk of delivering a LBW infant receives appropriate care.

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**Ethical clearance:** This work has been approved by the appropriate ethical committees related to the institution (Jawaharlal Nehru Medical College, Belgaum, India) in which it was carried out and the subjects have gave informed consent to the work.

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## References

1. Biswas R, Dasgupta A, Sinha RN, Chaudhuri RN. An epidemiological study of low birth weight newborns in the district of Puruliya, West Bengal. *Indian J Public Health* 2008;52:65-71.
2. Kumar A. Primary newborn care. *Health Action* 2002;15:5-6.
3. World Health Organisation, Development of indicators for monitoring progress towards "Health for all by year 2000". *Health for All Series*, No. 4, 1981, Geneva.
4. United Nations Children's Fund and World Health Organization, *Low Birth Weight: Country, regional and global estimates*. UNICEF, New York, 2004, p 1-9.
5. Agarwal AK. *Social Classification: The Need to Update*

- in the Present Scenario. *Indian J Community Med* 2008;33:50-1.
6. Mondal B. Low birth weight in relation to sex of baby, maternal age and parity: A hospital based study on Tangsa tribe from Arunachal Pradesh. *J Indian Med Assoc* 1998;96:362-4.
  7. Hirve SS, Ganatra BR. Determinants of low birth weight: A community based prospective cohort study. *Indian Pediatr* 1994;31:1221-4.
  8. Schlep FP, Pongpaew P. Analysis of low birth weight rates and associated factors in rural and urban hospital in Thailand. *J Trop Pediatr* 1985;31:4-8.
  9. Gebremariam A. Factors predisposing to low birth weight in Jimma Hospital south western Ethiopia. *East Afr Med J* 2005;82:554-8.
  10. Karim E, Mascie-Taylor CG. The association between birthweight, sociodemographic variables and maternal anthropometry in an urban sample from Dhaka, Bangladesh. *Ann Hum Biol* 1997;24:387-401.
  11. Chumnijarakij T, Nuchprayoon T, Chitinand S, Onthum Y, Quamkul N, Dusitsin N, et al. Maternal risk factors for low birth weight newborn in Thailand. *J Med Assoc Thai* 1992;75:445-52.
  12. Wang CS, Chou P. Risk factors for low birth weight among first-time mothers in southern Taiwan. *J Formos Med Assoc* 2001;100:168-72.
  13. Coutinho PR, Cecatti JG, Surita FG, Souza JP, Morais SS. Factors associated with low birth weight in a historical series of deliveries in Campinas, Brazil. *Rev Assoc Med Bras* 2009;55:692-9.
  14. Mavalankar DV, Gray RH, Trivedi CR. Risk factors for preterm and term low birthweight in Ahmedabad, India. *Int J Epidemiol* 1992;21:263-72.
  15. Stojanoviæ M, Bojaniæ V, Musoviæ D, Miloseviæ Z, Stojanoviæ D, Visujiæ A, et al. Maternal smoking during pregnancy and socioeconomic factors as predictors of low birth weight in term pregnancies in Nis. *Vojnosanit Pregl* 2010;67:145-50.
  16. Siza JE. Risk factors associated with low birth weight of neonates among pregnant women attending a referral hospital in northern Tanzania. *Tanzan J Health Res* 2008;10:1-8.
  17. Dinh PH, To TH, Vuong TH, Höjer B, Persson LA. Maternal factors influencing the occurrence of low birthweight in northern Vietnam. *Ann Trop Paediatr* 1996;16:327-33.
  18. Nair SN, Rao PRS, Chandrashekar S, Acharya D, Bhat VH. Socio-demographic and maternal determinants of low birth weight: A multivariate approach. *Indian J Pediatr* 2000;67:9-14.
  19. Janjua NZ, Delzell E, Larson RR, Meleth S, Kristensen S, Kabagambe E, et al. Determinants of low birth weight in urban Pakistan. *Public Health Nutr* 2009;12:789-98.
  20. Vega J, Sáez G, Smith M, Agurto M, Morris NM. Risk factors for low birth weight and intrauterine growth retardation in Santiago, Chile. *Rev Med Chil* 1993;121:1210-9.
  21. Park K. Preventive Medicine in Obstetrics, Paediatrics and Geriatrics. In: Park K, editor. *Text book of Preventive and Social Medicine 18<sup>th</sup> Ed.* Jabalpur: Banarsidas Bhanot Publishers; 2005. pp. 460.
  22. Tema T. Prevalence and determinants of low birth weight in Jimma Zone, Southwest Ethiopia. *East Afr Med J* 2006;83:366-71.
  23. Kalanda B, Verhoeff F, le Cessie S, Brabin J. Low birth weight and fetal anaemia as risk factors for infant morbidity in rural Malawi. *Malawi Med J* 2009;21:69-74.
  24. Rahmanifar A, Kirksey A, Mc Cabe GP, Galal OM, Harrison GG, Jerome NW. Respiratory tract and diarrheal infections of breast-fed infants from birth to 6 months of age in household contexts of an Egyptian village. *Eur J Clin Nutr* 1996;50:655-62.
  25. Tantracheewathorn S, Lohajaroensub S. Incidence and risk factors of iron deficiency anemia in term infants. *J Med Assoc Thai* 2005;88:45-51.

# A study of psychiatric co-morbidity in cases of renal failure, undergoing hemodialysis

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## Abstract

A study of patients with renal failure undergoing hemodialysis was conducted at renal dialysis unit and OPD of psychiatry department ,at Patna medical college & hospital to establish point prevalence of psychiatric co-morbidity in these patients. Patients of all age group, from all economic classes were recruited. Patients were assessed for common mental disorders using the MINI (MINI International neuropsychiatric interview). They were defined according to ICD 10/ DSM IV criteria. Total 60 patients were assessed in which 30 patients satisfied the criteria for the different common mental disorders. Hopelessness, restlessness, were most common presentation. Suicidal ideation was significantly associated with these patients.

## Keywords

Hemodialysis, GAD, Psychotic disorders

## Introduction

Patients with renal failure , on hemodialysis have been found to exhibit increased levels of psychological disturbances ( Scribner et al 1960, Maher et al 1960, Boen et al 1962, Hegstran et al 1960, Gutich et al 1964, Schumachar et al 1965, Schupak & Marrill 1965, Pendras & Erickson 1966, Ozcusemez G 2003, Pat et S.S shah V.S 2002) . Abram et al (1975) observed that sexual interest and ability are likely to be affected (Sensky T 1993, Levy 1975) in these patients. Psychiatric morbidity in patients undergoing hemodialysis is high and there is evidence that the suicide rate is above that of general population ( Siddiqui et al 1970, Abram 1971, Foeter et al 1973, Bruner 1976 & Kaplan 1876) .

## Materials and method

Study was performed on 60 cases of renal failure who were diagnosed clinically and on the basis of relevant investigations. They were admitted in renal dialysis unit of Patna medical college & hospital, Patna. Patients who were willing to participate, who could communicate verbally and were suitable for the hemodialysis were interviewed. Patients were selected from all age groups, from both sexes, from all communities, from all socio-economic class. Patients with previous history of mental

illness, not able to communicate and history of drug abuse were not included. Selected patients were assessed for common mental disorders using the MINI( It is a brief structured interview for major axis I disorders of DSM IV and ICD-10. Validation and reliability score of MINI is comparable to SCID or CIDI. It can be administered in much shorter period of time (mean 15 minutes). MINI is divided into modules identified by letters, each corresponding to a diagnostic category. At the beginning of each module, screening questions corresponding to main criteria of disorders are presented. At the end of each module, diagnostic boxes permit the interviewer to indicate that whether the diagnostic

Criteria have been met or not. Towards the end of study , collected datas were coded and tabulated in respective proformas and subjected to statistical analysis to answer the

{2} aims and objectives of this study. Analysis was done by applying CHI-SQUARE test and statistical significance was observed. Interview was done in 3 stages 1<sup>ST</sup> before starting the dialysis 2<sup>ND</sup> immediately after the dialysis 3<sup>RD</sup> during follow up in OPD & during intermittent dialysis. Interview included detailed history from patients and relatives, physical examination of the patients, pathological tests etc.

## Result & discussion

Sample consisted of 60 patients who fulfilled the inclusion and exclusion criterias. Control group of 60 patients were chosen from general medical wards with renal failure, but not on hemodialysis. Results are shown from Table no. 1- 5. Treatment of Chronic renal failure (CRF) by hemodialysis is a relatively new procedure which has been in use after 1960. It can prolong the life of patients who would have otherwise died due to their physical illness.

Aim of this study was to define and understand the stresses to which the average renal patients are subjected to. Underlying this aim was the hope that such understanding will lead in developing means of helping the patients undergoing hemodialysis in achieving an optimal adjustment. Patients reaction during dialysis were divided into 3 stages

- (a) Reaction before dialysis
- (b) Reaction during dialysis
- (c) Reaction after dialysis

Before the dialysis, patients shown increased incidence of apprehension, insomnia, irritability etc. During the dialysis,



patients were anxious, irritable and depressed. They often became aggressive and irritable. After the dialysis, there was sense of relief and hope. When Kaplan De Nour (1979) compared adolescent patients with adult patients, he observed that adolescent patients had poor compliance to diet and drugs with poor rehabilitation. They show more hostile attitude but less psychiatric complications and suicidal ideation than the adult patients. It was reported that patients with higher I.Q showed better co-operation, adjustment and rehabilitation. In the present study, we observed that if the patient adjust well, their family will probably have better reciprocal adjustment. Likewise if the family is able to react in a supportive manner the patient is certainly likely to benefit.

TABLE 1, Shows that psychiatric complications in the age group 41 – 60 is highest 51.7%, which can be explained due to increased liabilities with physical, social and economical stresses and strains of life being highest in this age group. This table also shows that greater number of cases being male. Salmons(1981) observed that men may find that their role in the family has changed. They are now dependent and this feeling may create psychiatric complications.

**Table 1:** Sample characteristics

Characteristics	study group	control group
1.Age groups(yrs)		
0-20	8(13.3%)	10(16.6%)
21-40	21(35%)	26(43.3%)
41-60	31(51.7%)	24(40%)
MEAN AGE	38.38+/- 12.94	35.5+/- 12.9
2. Gender		
Male	44(73.3%)	45(75%)
Female	16(26.6%)	15(25%)
3. Religion		
Hindu	42(70%)	45(75%)
others	18(30%)	15(25%)
4. Domicile		
Urban	45(75%)	44(73.3%)
Rural	15(25%)	16(26.6%)
5. Occupation		
Manual worker	10(16.6%)	24(40%)
Business	8(13.3%)	8(13.3%)
Others	42(70%)	28(46%)
6.Marital status		
Married	45(75%)	42(70%)
Unmarried	10(16.6%)	15(25%)
Divorced	5(8.3%)	3(4.9%)
7. Economic status		
Upper	21(35%)	15(25%)
Lower	39(65%)	45(75%)

Hindu patients constitutes the bulk of study group, which is explained by their more preponderance over other communities.

{ 3} TABLE 2, Shows that most common psychiatric symptoms were hopelessness, restlessness, sleeplessness,

loss of appetite. It was significant in comparison to control group.

**Table 2:** Chief Psychiatric sign's and symptom's of Patients

Complaints	Study group	Control group
Hopelessness	22(73.3%)	2(16.6%)
Restlessness	22(73.3%)	2(16.6%)
Sleeplessness	21(70%)	3(25%)
Loss of appetite	22(73.3%)	3(25%)
Aggressiveness	21(70%)	2(16.6%)
Suicidal ideation	16(53.33%)	2(16.6%)
Fear of death	10(33.3%)	2(16.6%)
Guilt	08(26.6%)	2(16.6%)
Loss of libido	07(23.3%)	2(8.33%)
Irrelevant speech	5(16.6%)	1(8.33%)
Delusion	05(16.6%)	NIL
Hallucination	05(16.6%)	NIL

TABLE 3, Shows most common psychiatric diagnosis: GAD, Depression, Organic brain syndrome. Gordon et al (1973) found that 47% of their patients suffered from intermittent depression. Kaplan (1971) observed 53% of patients were depressed.

**Table 3:** Psychiatric disorders in hemodialysis patients

Disorder	Study group	Control group
G AD	12(40%)	4(33.3%)
Depression	11(36.66%)	4(33.3%)
Psychosis	2(6.66%)	NIL
Org. brain syndrome	5(16.6%)	4(33.3%)

TABLE 4, Shows that 40% of patients developed psychiatric complications during first 20 sessions of dialysis. Later incidence decreases due to better understanding.

**Table 4:** Correlation of Psychiatric complications with no. of dialysis session

No. of dialysis session	No. of cases showing psych.complications	Percentage (%)
1-20	12	40%
21-40	10	33.30%
41-60	08	26.60%

TABLE 5, Shows that maximum 40% of patients developed psychiatric complications during first 4 months of intermittent dialysis. Reichsman (1972) observed 3 distinct stages during maintenance hemodialysis

**Table 5:** Correlation of Psychiatric complications with duration of hemodialysis

Duration to develop Psych. complications	No. of cases showing psych.complications	Percentage (%)
0- 4 months	13	43%
5- 8 months	10	33.30%
9- 12 months	07	23.10%

- (a) Honeymoon “ period
- (b) Period of discouragement
- (c) Period of long term adaptation

Onset of 1<sup>st</sup> stage occurs 1-3 weeks after the 1<sup>st</sup> hemodialysis with duration ranging from 6 weeks to 6 months. During this stage patients had full hope and confidence.

2<sup>nd</sup> stage-all confidence and hope disappeared and they became helpless and sad. It lasted for 3-12 months.

In the 3<sup>rd</sup> stage patients accept their limitations and start adapting with circumstances.

Denial is seen as the most commonly used defence mechanism by the dialysis patients. The attitude of staff members seems to be the most important factor in the management of these patients. Their co-operation makes dialysis patients more adjustable.

## CONCLUSION

Psychiatric morbidity was significantly higher in patients with renal failure on hemodialysis, than in those who were not on hemodialysis. Hopelessness and GAD were the most common psychiatric morbidity associated with. Majority of psychiatric complications appeared during first 20 sessions of hemodialysis within 4 months.

## References

1. Abram H.S. The psychiatrist, the treatment of chronic renal failure and the prolongation of life part I, Am.J. Psychiatry, 1968;124:10,45-52,
2. Foster G.G, Chon G.L , Mckezney F.P. Psychological factors and individual survival on chronic renal hemodialysis, 2yrs follow up part I, Psychosom, med, 1973,35:1, Jan- Feb.
3. Kaplan de nou, Adolescents adjustment to chronic hemodialysis, Am.J.Psychiatry, 1979,136, April.
4. Maher J.F, Schreiner G.E, Waters T.J, Successful intermittent hemodialysis- longest reported maintenance of life in true oliguria (181 days) Tr.Am.Soc.Int.Org, 1960,6:123-27.
5. Patel SS, Shah VS, Psychosocial variables, quality of life and religious beliefs in ESRD patients treated with hemodialysis, Am. J. Kidney dis. 2002, 40(5):1013-22
6. Reichman E, Levy N.B , Problems in adaptation to maintenance hemodialysis, Arcs Int. Med, 1972 130, 859-65.
7. Siddiqui J.Y, Fitz A.E, J.A.M.A, 1970, 212, 1350.
8. Gordon F F, Psychobiologic factors on chronic renal failure, follow up, Part-I
9. Winokur M.Z, JW Kaplan, Intelligence and adjustment to chronic hemodialysis, Psychosom Res, 1973, 17: 29-34.

# A rare case of recurrent desmoplastic ameloblastoma of maxilla

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## Abstract

Desmoplastic ameloblastoma (DA) is a benign, locally invasive variant of the intraosseous, infiltrative ameloblastoma (IA). Ameloblastoma, of the maxilla, has a bad reputation with a high recurrence rate and significant mortality. For a benign tumor, which should be a curable condition, this seems to be out of character. We present a case of recurrent maxillary desmoplastic ameloblastoma and discuss the clinical features, pathology and management of these lesions and review the literature.

## Keywords

Desmoplastic , Ameloblastoma, Maxilla, Partial maxillectomy.

## Introduction

The ameloblastoma is notorious for its slow growth, the histologically benign appearance, local invasiveness and a high incidence (50–72 per cent) of local recurrence occurring most often in the mandible, and less commonly in the maxilla and peripheral sites.<sup>1</sup> DA is a benign epithelial neoplasm believed to be a variant or subtype of the intraosseously located, infiltrative (conventional) ameloblastoma (IA). The tumor is among several features characterized by an unusual histomorphology, including extensive stromal collagenization or desmoplasia; hence the term proposed for this variant: ameloblastoma with pronounced desmoplasia, or, for short *desmoplastic ameloblastoma* (DA).<sup>2</sup> Ameloblastoma is uncommon in the maxilla, comprising about 15% of all reported ameloblastomas. In the maxilla, 47% of ameloblastomas have been reported in the molar region, 15% in the maxillary antrum and floor of the nose, 9% in the premolar region, 9% in the canine and incisor region and 2 % in the palate. Maxillary ameloblastomas, while histologically indistinguishable from their mandibular counterparts, may behave aggressively and are considered inherently more difficult to manage. The proximity of the maxilla to the orbit, skull

base and intracranial contents accounts for most of the deaths attributed to ameloblastomas in this site.<sup>3</sup>

## Case report

A male (40 years) underwent excision of a solid lesion and extraction of teeth 21 to 25 in Nov, 2000. The histological report was not maintained by the patient but in discharge summary it was mentioned as ameloblastoma. Since Feb 2009 he was aware of a slowly progressive, painless swelling over the upper right half of the face. There was asymmetry of the mid-face, with a painless swelling with obliteration of nasolabial fold and raised ala of nose on right side (figure-1). Intraoral examination revealed a painless swelling both on the buccal and palatal aspect from 16 to the left alveolar ridge of the maxilla till the resected portion previously without any ulceration. Clinical and neurological examinations did not reveal any abnormality. There was no evidence of spread of the disease to regional lymph nodes nor distant metastasis as confirmed by scan (figure-3). Occlusal and panoramic radiographs disclosed a diffuse, poorly delineated moth-eaten radiolucent/radiopaque lesion of the anterior maxilla from right second premolar to left second premolar (15 to 25). CT scans showed a lytic tumor adjacent to the alveolar ridge of anterior maxilla from second premolar to second premolar (15 to 25) extending into the sinus (figure-2). A biopsy revealed diagnosis of ameloblastoma. In September 2009, he underwent partial maxillectomy along the Le Fort I plane from the right first molar region to left first molar region along with excision of sinus lining bilaterally. The operation specimen was a solid mass, which measured 6 x 6 x 2.5 cm. Histopathological report revealed a completely resected desmoplastic ameloblastoma (figure-4). The patient received a definite obturator after refusing bony reconstruction with 1 year follow up, without any signs of recurrence (figure-5).

## Discussion

DA is a benign, locally invasive variant of the intraosseous, infiltrative ameloblastoma (IA). A painless swelling represents the chief initial complaint in most cases.<sup>2</sup> Other symptoms are resorption of roots, toothache, malocclusion, pathological fracture, pain or numbness<sup>4</sup>. The size of the tumour varies between 1.0 and 8.5 cm at the greatest diameter. The DA accounts for 4-13% of all ameloblastomas. The over-all average age is 42.9 years,

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**Figure 1:** Preoperative photograph showing swelling of right side of upper face and raised ala of nose.



**Figure 2:** Axial and 3 D CT scan



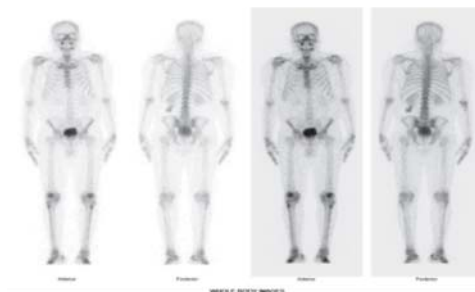
**Figure 5:** Postoperative photograph with obturator.



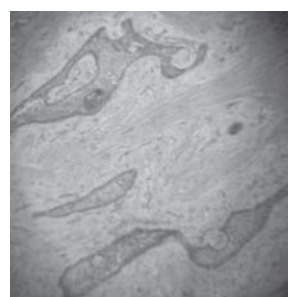
higher for males (45.9 years) than for females (39.7 years). The male/female ratio is 1:1. The maxilla/mandible ratio is 1/0.9 as opposed to 1/5.4 for the IA.<sup>2</sup> It was noteworthy that desmoplastic ameloblastomas were often seen in the maxillary sinus (25%) and incisor segments (62.5%).<sup>5</sup> As lack of early symptoms of a maxillary ameloblastoma, the patient usually consults the doctor at a time when the tumor already extends beyond the confines of the maxilla. The fact that cortical bone is rare in the maxilla and the intimacy with the nasal cavity, paranasal sinuses, orbits, parapharyngeal tissues and the vital structures at the skull-base make obvious the totally different growth pattern of maxillary ameloblastomas in contrast to those of the mandible.<sup>6</sup>

The theories of pathogenesis of the ameloblastoma summarized the four possible sources of cells that could give rise to these lesions, as follows: (a) the epithelial lining of an odontogenic cyst; (b) dental lamina or enamel organ; (c) stratified squamous epithelium of the oral cavity; and (d) displaced dental epithelial remnants.<sup>7</sup> The radiographic

**Figure 3:** Postoperative bone scan showing no distant metastasis.



**Figure 4:** Tumour islands are large with squamatoid epithelial cells and micro-cyst formation. Stromal desmoplasia is seen (H&E X10)



features of DA differ in most cases from those of IA. The DA shows ill-defined borders with a soap bubble appearance with the finding of a mixed radiolucency-radiopacity. The fact that new bone formation and infiltrative pattern of the tumour may explain the mixed radiolucent/radio-paque appearance<sup>8</sup>. Histologically, the most striking feature separating the DA from IA is to be found in the tumour stroma: It consists of proliferating, irregularly shaped islands and narrow cords of odontogenic epithelium of varying sizes embedded in a desmoplastic, connective tissue stroma. The occasional large tumour islands are often very irregular in shape with a pointed, stellate or "kite-like" appearance. The morphology of these islands is usually bizarre with "animal-like" configurations. The epithelial cells at the periphery of the islands are cuboidal, occasionally with hyperchromatic nuclei. Columnar cells demonstrating reversed nuclear polarity are rarely conspicuous although an occasional isolated island may show ameloblast-like peripheral cells focally. The center of the epithelial islands may appear hypercellular with spindle-shaped or squamatoid epithelial cells. Micro-cysts containing eosinophilic amorphous deposits or appearing empty are commonly found within the tumour islands. Extensive stromal desmoplasia is a constant and striking finding characterized by a moderately cellular fibrous connective tissue with abundant thick collagen fibres that seems to compress or "squeeze" the odontogenic epithelial islands from the periphery.<sup>2</sup>

Management of the ameloblastoma has variously included

chemotherapy, electrocautery, cryosurgery, radiotherapy, conservative curettage and radical block excision. Joseph and Savage (1992) mentioned that the more abundant blood supply of the maxilla may also aid in local haematogenous spread of the neoplasm.<sup>6</sup> The current treatment of choice is a maxillary resection (approached like a Le Fort I osteotomy and downfracture or conventional) with a 10–15mm margin of bone including the entire alveolar ridge and hard palate, as well as removal of the mucous membrane of the entire maxillary sinus and lateral wall of the nose.<sup>9</sup> In our study, we did not observe metastasis, although this could appear over a longer time period. Because of relative confusion as to how maxillary ameloblastoma should be treated, a classification has been developed<sup>10</sup>.

Group 1. Tumours confined to the maxilla without involvement of the orbital floor.

Group 2. Tumours involving the orbital floor, but not the periorbital area.

Group 3. Tumours involving the orbital contents.

Group 4. Tumours involving the skull base.

The treatment indicated in each group is as follows:

Group 1. Partial maxillectomy.

Group 2. Total maxillectomy.

Group 3. Total maxillectomy with orbital exenteration.

Group 4. Total maxillectomy with anterior skull base resection and orbital exenteration as indicated

According to the WHO-classification possibly desmo-plastic ameloblastoma have lower recurrence rates than other ameloblastomas. The answer can be given only when more information accumulates in the literature.<sup>2</sup> Recurrences developed at an average time interval of 7.2 years<sup>5</sup> as fits with our case. Sehdev et al. after reviewing 20 patients with maxillary ameloblastoma seen over 50 years have demonstrated that curettage was followed by local recurrence in 90 per cent of mandibular and 100 percent of maxillary ameloblastomas<sup>11</sup>. It is claimed that curettage opens pathways for the spread of tumour to adjacent structures and that could be a reason for recurrence in this case after curettage of initial lesion.<sup>4</sup>

## Conclusion

The biological behaviour of the DA including recurrence rate still can not be fully appreciated due to the relative few reported cases with sufficiently long follow-up periods. It is suggested that rare subtypes of ameloblastoma such

as the desmoplastic ameloblastoma and others should be published as case reports or smaller series for definite conclusions to be drawn.

## References

1. Infante-Cossio P, Hernandez-Guisado JM, Fernandez-Machin P, Garcia-Perla A, Rollon Mayordomo A, Gutierrez-Perez JL: Ameloblastic carcinoma of the maxilla: a report of 3 cases. *J Cranio-Maxillofac Surg* , 1998;26: 159–162.
2. H.P. Philipsen et al : Desmoplastic ameloblastoma (including “hybrid” lesion of ameloblastoma). Biological profile based on 100 cases from the literature and own files. *Oral Oncology* 2001; 37:455-460
3. A. L. Nastri, D. Wiesenfeld, B. G. Radden, J. Eveson, C. Scully .Maxillary ameloblastoma: a retrospective study of 13 cases. *British Journal of Oral and Maxillofacial Surgery* 1995 ;33: 28-32.
4. Shatkin S, Hoffmeister FS: Ameloblastoma: a rational approach to therapy. *Oral Surg Oral Med Oral Pathol* 1965;20: 421–435.
5. P.A. Reichart, HP. Philipsen and S. Sonner. Ameloblastoma: Biological Profile of 3677 Cases. *Oral Oncol, Eur J Cancer*, 1995;Vol. 31B, No. 2, pp. E&99.
6. Roger Arthur Zwahlen, Klaus Wilhelm Gratz. Maxillary ameloblastomas: a review of the literature and of a 15-year database. *Journal of Cranio-Maxillofacial Surgery* 2002; 30, 273–279.
7. D Bray, A Michael, D T Falconer, H S Kaddour. Ameloblastoma: a rare nasal polyp. *The Journal of Laryngology & Otology* 2007;121:72–75.
8. Takata T, Miyauchi M, Ito H, et al. Clinical and histopathological analyses of desmoplastic ameloblastoma. *Pathology Research Practice* 1999;195: 669-75.
9. Sailer HF, Haers PE, Gratz KW: The Le Fort I osteotomy as a surgical approach for removal of tumors of the midface. *J Cranio-Maxillofac Surg* 1999; 27: 1–6.
10. I. T. Jackson, P. P. Callan, Robert A. An anatomical classification of maxillary ameloblastoma as an aid to surgical treatment. *Cranio-Maxillofacial Surgery* 1996; 24:230-236.
11. Sehdev MK, Huvos AG, Strong EW, Gerold FP, Willis GW: Proceedings: Ameloblastoma of maxilla. and mandible. *Cancer* . 1974;33: 324–333.

# Ultrasonic measurement of foetal biparietal diameter and its correlation to gestational age in the Garhwali population

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## Abstract

Accurate knowledge of the maturity of the foetus influences management of antepartum care of a patient, planning of appropriate therapy or intervention, perinatal morbidity and mortality. Measurement of Biparietal diameter by ultrasound has proved to be a useful and accurate method for determining gestational age and maturity of the foetus. In the present study foetal Biparietal diameter was measured in 25 Garhwali women during normal pregnancy between 12-40 weeks of pregnancy and noted that the mean Biparietal diameter of cranium between 12-16 weeks of gestation was  $29.74 \pm 4.95$  mm and it attained a maximum mean of  $90.58 \pm 2.68$  at full term pregnancy (36-40 weeks). This study showed that the gestational age calculated from the regression equation for the Biparietal diameter correlates well with the actual gestational age, so biparietal diameter is a good parameter for assessing maturity of the foetus.

## Keywords

Biparietal Diameter, Gestational Age.

## Introduction

Historically the patient's last menstrual period (LMP) was the first method of gestational dating. Unfortunately, this method cannot be used for all patients because 10-40% of the patients seen in prenatal clinics either have no knowledge of their LMP or have a history of irregular menstrual cycles or have conceived while on oral contraceptives. For these patients other methods of gestational dating like uterine size measurement and quickening must be used but these are less accurate. Measurement of Biparietal diameter by ultrasound has proved to be a useful and more accurate method for determining gestational age of the fetus. Ultrasonic measurement of the biparietal diameter in utero was introduced by Donald<sup>1</sup> in 1959 and first reported in 1961. Campbell & Newman<sup>2</sup> (1971) stated that the foetal BPD can be measured Ultrasonologically 13<sup>th</sup> week of pregnancy onwards.

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Ultrasonic measurement of biparietal diameter gives misleading conclusion due to the different craniofacial dimensions in the various races. It is reported by Williams et al<sup>3</sup> (1995) that the shape of the vault is not directly related to cerebral growth but to the genetic factors. In the passed various other workers (Campbell & Newman<sup>2</sup> 1971; Varma<sup>4</sup> 1973; Sabbagha et al<sup>5</sup> 1974; Parker et al<sup>6</sup> 1982; Okupe et al<sup>7</sup> 1984; Rajan<sup>8</sup> 1996; Rajlakshmi et al<sup>9</sup> 2001) measured biparietal diameter ultrasonographically in the various races all around the world and correlated it to the gestational age.

In Uttaranchal six tribal communities have been found. The present study was done in Bhotia, Boksa, Tharus and Raji tribes of Garhwali population, which were coming from Pauri, Tehri, Uttarkashi and Dehradun.

## Aims & objective

In this study determination of foetal cephalic parameter i.e. biparietal diameter was done by ultrasonography and its correlation with gestational age was done in the Garhwali population.

## Material and methods

The study was conducted on 25 pregnant women of Garhwal region, visiting the Himalayan Institute Hospital (HIMS), Swami Ram Nagar, Dehradun.

The subjects chosen for the study met the following criteria:-

- I. Singleton pregnancy
  - II. Good menstrual dating that is, regular menstrual cycles 28 to 31 days, has a known LMP .
  - III. The physical examination tallied with the menstrual dating.
  - IV. There was no history of medical or obstetrics complications.
  - V. At Least the patient or her husband was a native of Garhwal region
  - VI. No gross congenital anomaly of the foetus especially in the regions of the head and lower limb.
- A.** Appropriate transverse axial plane of section for measurement of the fetal biparietal diameter.  
F- Falx, CSP- Cavum septi pellucidi, T- Thalamic nuclei, CP- Choroid plexus
- B.** BPD measurement from outer edge to inner edge of skull table denoted by arrow heads and dotted line. In this study, the fetal cephalometry was performed

by measuring the biparietal diameters of the fetuses at different gestational ages on a Siemen's Sonographic equipment. Every patient had gone at least three serial measurements. In making BPD measurement, the fetal head should be imaged in a transverse axial section. Intracranial landmarks should include the falx cerebri anteriorly and posteriorly, the cavum septi pellucidi anteriorly in the midline, and the choroid plexus in the atrium of each lateral ventricle and bilateral thalamic nuclei. The BPD is measured from the outer edge of the skull table nearest the transducer to the inner edge of the opposite skull table, perpendicular to the midline (Fig A&B).

All the Gestational Ages were calculated from the date of LMP. The mean of the biparietal diameters with their standard deviation, standard error and 95% confidence level were calculated. The correlation of Biparietal diameters of the cranium with their gestational ages were tabulated. From the above data mean growth rates of the Biparietal diameter were calculated and the linear regression equation of the above parameter was derived.

### Observation & results

Table I shows that the mean BPD of cranium between 12-16 weeks of gestation was  $29.74 \pm 4.95$  mm it attained a maximum mean of  $90.58 \pm 2.68$  mm at full term pregnancy i.e. 36-40 weeks. Table I also shows that the mean growth rate of BPD was 3.8 mm per week at 12-16 weeks which approached to 1.6 mm per week at full term pregnancy (36-40 weeks). Mean BPD of cranium of fetuses correlated well with the gestational age with a positive correlation coefficient (r) of 0.98 (Table I).

Graph I shows that as the gestational age increases, the

**Table I:** Mean biparietal diameter and mean growth rate of biparietal diameter of cranium with increasing gestational age

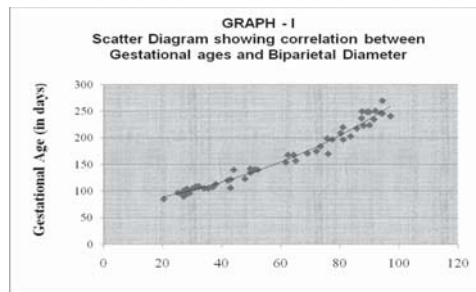
Gestational Age In Weeks (n)	Mean Biparietal Diameter (in mm) $\pm$ S.D.	Biparietal Diameter(mm)
12-16 (19)	$29.74 \pm 4.95$	3.8
16-20 (9)	$41.93 \pm 6.94$	5.5
20-24 (5)	$58.08 \pm 6.77$	6.1
24-28 (6)	$69.52 \pm 5.32$	4.6
28-32 (7)	$80.67 \pm 3.41$	4.0
32-36 (7)	$90.30 \pm 4.50$	1.9
36-40 (5)	$90.58 \pm 2.68$	1.6

n = No. of cases                      S.D. = Standard Deviation  
t = 4.56                                      p = < 0.05  
r (correlation coefficient between gestational ages & Mean BPD) = 0.98

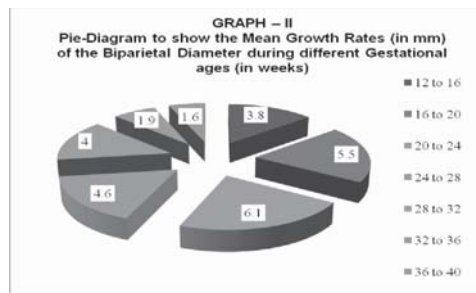
mean BPD increases. This graph shows the linear growth pattern of BPD. Graph II shows that the maximum growth rate was 6.1 mm per week during the 20-24 weeks and the minimum growth rate was 1.6 mm per week during 36-40

**Graph 1:**

$$y = 32.7385 + 2.2003x$$



**Graph 2:**



weeks. The regression equation showing the correlation between gestational age and BPD is  $y = 32.7385 + 2.2003x$  where y denotes the gestational age in days and x denotes the BPD in mm. The equation shows that with the increase of 1mm in BPD there was an advancement of 2.2003 days (0.3143 week) of gestational age.

Table II shows that the Gestational age calculated from the regression equation of BPD correlated well with the actual gestational age (from LMP) to within 1-2 weeks during 12-36 weeks but after 36 weeks the correlation decreases specially in the late third trimester, when the difference between gestational age calculated from the regression equation and actual gestational age is approximately four weeks.

### Discussion

Varma<sup>4</sup> (1973), observed a progressive increase in the BPD at least upto 40 weeks. Sabbagha et al<sup>10</sup> (1976) noted that the curves for the BPD in Negroid and European population were similar although minor differences were there in the foetal age distribution beyond 23 weeks. . Parker et al<sup>6</sup> (1982) reported that there was no significant differences in the BPD of Asian and European foetuses Dubowitz & Goldberg<sup>11</sup> (1981) studied fetuses of Caucasian, Negro, Indian and mixed origins but found no significant differences in Biparietal Diameter (BPD) except after 30 weeks of gestation. Okupe et al<sup>7</sup> (1984) measured BPD in Nigerian women during normal pregnancy and showed that the growth of BPD in the Nigerian population showed asymptotic curve like that of Europeans but their values were slightly higher.

**Table 2:** Gestational age calculated from Imp & regression equation

Range of Gestational Age (In Weeks)	Biparietal Diameter (in mm)	Gestational Age (in Days) from LMP	Gestational Age (in Days) from Regression Equation	Difference between 3 <sup>rd</sup> & 4 <sup>th</sup> Column reading (Days)
12-16	26.20	96	102	6
16-20	32.20	109	118	9
20-24	50.40	138	148	10
24-28	72.00	175	191	16
28-32	81.10	197	211	14
32-36	87.30	237	224	13
36-40	92.00 94.40	251 270	234 240	17 30

**Table 3:** Mean biparietal diameter (in mm)

Author	Weeks of Gestational age						
	12-16	16-20	20-24	24-28	28-32	32-36	36-40
Tuli <sup>13</sup> (1995)	18	26	31	46	53	63	63
Rajan <sup>8</sup> (1996)	30	41	52	65	75	82	87
Rajlakshmi <sup>9</sup> (2001)	28.1	39.5	46.8	59.4	70.0	80.0	87.8
Present Study	29.74	41.93	58.08	69.52	80.67	90.30	90.58

**Table 4:** Growth rate of bpd (mm per week)

Author	Weeks of Gestational age						
	Up to 30 weeks				After 30 weeks		
Willocks <sup>14</sup> (1964)	-				1.6		
Thompson <sup>15</sup> (1965)	-				1.8		
Campbell <sup>16</sup> (1969)	2.8				1.5		
Varma <sup>4</sup> (1973)	2.73				1.67		
Rajlakshmi <sup>9</sup> (2001)	12-16	16-20	20-24	24-28	28-32	32-36	36-40
	2.5	2.6	1.6	6.6	4.0	5.1	6.1
Present Study	3.8	5.5	6.1	4.6	4.0	1.9	1.6

Asthana et al<sup>12</sup> (1995) after a study in the Allahabad population found that the growth of the BPD was linear. Rajlakshmi et al<sup>9</sup> (2001) after a study in the Manipuri population noted that the mean BPD increases from 12-14 weeks of gestation i.e. 28.1±5.3 at 12-16 weeks to 87.8±3.8 at full term. They showed that with an increase of 1mm of BPD the gestational age increased by 2.45 days (0.35 weeks). In the present study the mean BPD increased from 29.74±4.95 (12-16 weeks) to 90.58±2.68 at full term (36-40 weeks). Our study showed that with an increase of 1mm of BPD, the gestational age increased by 2.2003 days (0.3143 weeks).

Table IV shows that the Campbell (1969) & Varma (1973) observed higher growth rate upto 30 weeks and slower growth rate 30-40 weeks. In our study too higher growth rate observed upto 32 weeks and slower growth rate from 32-40 weeks.

Bowie & Andreotti<sup>17</sup> (1983) stated that the degree of variation in biparietal diameter results from racial or socioeconomic differences, maternal disease or fetal head shape. They believe that the optimal determinations are obtained from 15-26 weeks, that from 27-30 weeks there is a progressive increase in variability and after 30 weeks satisfactory assignment of gestational age is difficult.

Hadlock et al<sup>18</sup> (1981) stated that the range of error in predicting gestational age by the BPD varied from 1.5 weeks in second trimester to 5.5 weeks in the late third trimester. Gupta<sup>19</sup> (2001) stated that a single optimal measurement of the BPD will predict the gestational age to within ± 10 days from 14-26 weeks ± 14 days from 27-28 weeks and ± 21 days from 29-42 weeks.

Our study showed that BPD has proved to be a reliable indicator of foetal gestational age upto 36 weeks but in the late third trimester the reported accuracy is less (Table II) similar to the results of Hadlock<sup>18</sup> & Gupta<sup>19</sup>.

Sabbagha<sup>5</sup> (1974) showed that with 95% confidence level gestational age varies ±11 days. Asthana et al<sup>12</sup> (1995) noted that with 96% confidence level gestational age varies ± 10 days. Berger et al<sup>20</sup> (1975) stated that for a given BPD, gestational age can be estimated within about ± 1 week with a confidence of only 50% or within about ± 2 weeks with a confidence of about 90%. Wennerholm et al<sup>21</sup> (1998) stated that the mean gestational age calculated from the ultrasound measurements was significantly shorter than the mean gestational age estimated from the day of oocyte retrieval. The mean difference was 1.9 days (SD 3.3); 95% CI 1.5-2.4.

Our study proved the confidence level 95% ±14 days



## Conclusion

Gestational age calculated from the regression equation of BPD correlated well with the actual gestational age (from LMP) to within 1-2 weeks during 12-36 weeks but after 36 weeks correlation decreased.

## References

1. Donald I, Brown TG: Demonstration of tissue interfaces within the body of ultrasonic echo sounding: *Br J Radiol* 1961; 34:539.
2. Campbell S. and Newman GB. Growth of the fetal biparietal diameter during normal pregnancy. *The Journal of Obstetrics and Gynaecology of the British Commonwealth* 1971; 78:513-519.
3. William PL, Dyson M, Dussek JE, Bannister LH, Berry MM, Collins P et al. Skeletal system. In: *Gray's Anatomy*, 38<sup>th</sup> edition. Edinburgh, London: ELBS; 1995. p. 607-12.
4. Varma TR. Prediction of delivery date by ultrasound cephalometry. *The Journal of Obstetrics and Gynaecology of the British Commonwealth* 1973; 80: 316-319.
5. Sabbagha RE, Turner JH, Rockette H, Mazer J and Orgill J. Sonar BPD and fetal age. *Obstetrics and Gynaecology* 1974; 43 :7-13.
6. Parker AJ, Davies P, Newton JR. Assessment of gestational age of Asian fetus by the sonar measurement of crown-rump length and biparietal diameter. *British Journal of Obstetrics & Gynaecology* 1982; 89: 836- 838.
7. Okupe RF, Cooker OO, Gbajumo SA. Assessment of foetal biparietal diameter during normal pregnancy by ultrasound in Nigerian women. *British Journal of Obstetrics and Gynaecology* 1984; 99: 629-632.
8. Rajan R; Fetal biometry. *Ultrasonic in obstetrics, gynaecology and infertility*. 2<sup>nd</sup> ed. New Delhi: CBS publishers and Distributors; 1996. p. 181-94.
9. Rajlakshmi C, Singh SM, Devi B and Singh CL. Cephalic Index of foetuses of Manipuri population –A Baseline study. *Journal of The Anatomical Society of India* 2001; 50: 8-10.
10. Sabbagha RE, Barton FB and Barton BA. Sonar biparietal diameter. Analysis of percentile growth differences in two normal population using same methodology. *American Journal of Obstetrics and Gynaecology* 1976;126:479-484.
11. Dubowitz LMS and Goldberg C. Assessment of gestation by ultrasound in various stages of pregnancy in infants differing in size and ethnic origin. *British Journal of Obstetrics and Gynaecology* 1981; 88: 225-259.
12. Asthana AK, Singh AK, Kumar V et al. Assessment of gestational age by ultrasonographic measurement of biparietal diameter in utero. *Journal of Anatomical Sciences* 1995; 14(2): 1-5.
13. Tuli A, Choudhary R, Agarwal S, Anand C and Garg H. Correlation between craniofacial dimension and fetal age. *Journal of the Anatomical Society of India* 1995;44: 1-12.
14. Willock J, Donald I, Duggan TC and Day N. *Obstet Gynaecol British Commonwealth* 1964; 71:11.
15. Thompson HE, Holmes JH, Gottesfeld KR and Taylor ES. *American Journal of Obstetrics and Gynaecology* 1965;92:44.
16. Campbell S. The prediction of foetal maturity by ultrasonic measurements of biparietal diameter. *Journal of Obstetrics and Gynaecology, British Commonwealth* 1969; 76: 603-609
17. Bowie JD and Andreotti RF. Estimating gestational age in utero. In: Callen P, editor. *Ultrasonography in Obstetrics and Gynaecology*. Philadelphia : WB Saunders Company; 1983. p. 21-39.
18. Hadlock FP, Deter RL, Carpenter RJ and Park SK. Estimating fetal Age : Effect of head shape on BPD. *American Journal of Radiology* 1981; 137:83-85.
19. Gupta K. Measurement of fetal parameters. In: Malhotra N, Kumar P, Gupta DS, Rajan R, editors. *Ultrasound in Obstetrics and Gynaecology*. 3<sup>rd</sup> ed. Delhi: Jaypee Brothers Lordson Publishers; 2001. p. 92-8.
20. Berger GS, Edelman DA and Kerenyl TD. Fetal crown rump length and biparietal diameter in the second trimester of pregnancy. *American Journal of Obstet. Gynaecol* 1975; 9-12.
21. Wennerholm UB, Bergh C, Hagberg H, Sultan B and Wennergren M. Gestational age in pregnancies after in-vitro fertilization: Comparison between ultrasound measurement and actual age. *Ultrasound Obstet Gynecol* 1998;170-174.

# Angelman syndrome - A rare case report

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## Abstract

Angelman Syndrome (AS) was first described in 1965 as "puppet children" characterized by severe neuro-developmental disability, inability to speak, abnormal motor movement, easily provoked laughter, and epilepsy. Particular mechanisms identified as leading to Angelman Syndrome include deletions of part of the maternally inherited copy of chromosome 15.

Here with we report a case of 14 year old girl with Angelman syndrome who presented to the department with complain of painful teeth.

## Keywords

Angelman syndrome, chromosome 15 deletions, mental retardation, behavioral abnormalities.

## Synonyms

Happy puppet syndrome

## Introduction

Angelman syndrome (AS) is a distinct neurogenetic syndrome, first described by Dr Harry Angelman in 1965, an English paediatrician.<sup>1</sup> Angelman syndrome is a neurogenic disorder that affects the brain and causes a pattern of clinical features including delayed motor activities such as walking or ataxic gait, mental retardation with minimal or absent speech, seizures sleep disturbances, characteristic facial features and happy demeanor with specific EEG abnormalities.<sup>2</sup> Orofacial features include, microcephaly, macrostomia, maxillary hypoplasia, prognathism and neurological problems. Patients have a happy and excitable personality.<sup>1</sup>

## Case report

A young girl aged about 14 years was brought by her mother to the Department of Oral Medicine and Radiology, Bapuji Dental College and Hospital, Davangere, complaining of pain in right lower back teeth region since

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15 days. Patient was healthy with happy demeanor and frequent laughter. Her mother revealed that she is mentally retarded since birth. Her birth history revealed, delay in the development of both motor and language skills. Her head control was acquired at 5<sup>th</sup> month; she started rolling over at 6<sup>th</sup> month, and first sat at 8<sup>th</sup> month, started walking without support at 1 year 6 months and speech started at 2 years. There was no history of seizures. Her family history revealed that there was no history of consanguineous marriage between her parents and she had one younger sister and brother with no known developmental defects. There was no complication during pregnancy and she was born at term weighing 3.5 kgs with jaundice at 3<sup>rd</sup> day of her birth, which was treated. Her oral hygiene habits revealed that she brushes her teeth once daily with toothbrush and paste. She attained Menarche at the age of 14 years.

Her past medical history revealed, that, her psychological analysis done at Shristi Special Academy, Bangalore at the age of 4 years revealed mental age was of 1-year 6months, IQ 40, social development was below 2 years, motor development was of 3 years; cognitive development was below 2 years with moderate mental retardation. Her educational performance at the age of 6 years was unsatisfactory. Binnet Kamat test of intelligence (BKT) done at St. Johns Medical College and Hospital at the age of 7 years she obtained an IQ of 59, indicating her mental age was 4 years. Currently she has a vocabulary of using approximately 5-6 words. She was described as having very short attention span, and being physically active. She was having attraction and fascination with water. Her previous laboratory test report done at Bangalore 4 months back revealed, decreased hemoglobin- 9.8 gms/dl, raised serum alkaline phosphatase level- 375.9 U/l, elevated serum Albumin: Globulin ratio was 1.1:1. All other Laboratory investigations were within normal limits.

On general physical examination she was moderately built and nourished. She had ataxic gait. There was no pallor; icterus, cyanosis, clubbing, edema and all her vital signs were within normal limits. She was well oriented with time and place but was not obeying commands of her mother and had happy demeanor expression. Solitary bilateral submandibular lymph nodes palpable on right and left side, measuring about 0.5cmx0.5cm, mobile, firm and non-tender.

On Extra oral examination, she has thick medial eyebrows, hypertelorism, upslant eyes with left side ptosis,

Strabismus, bilateral cup shaped ears, flat philtrum, wide mouth (photograph 1), and prominent chin (photograph 2). On Intra oral examination, normal compliment set of teeth were present. She had narrow high arched palate ( photograph 3), a root stump with respect to 46 (photograph 4), labially placed 15, palatally placed 14(photograph 3). Radiographs could not be taken, as patient was uncooperative. Clinically by her past medical history, her behavior and by clinical presentation we considered it as a case of Angelman syndrome as the features were similar to the cases reported in the available literature. A provisional diagnosis as chronic periapical abscess with respect to 46 was made.

A second opinion of expert Pediatrician was taken for general evaluation, her sub normal behavior, clinical presentation and extra oral examination, which depicted again as a case of Angelman syndrome. Later patient was referred to the department of Pedodontics. Her root stump was extracted under general anesthesia in the Department of Oral and Maxillofacial Surgery under general anesthesia. Blood sample was taken at the same time and was sent for genetic analysis to Sir Gangaram Hospital, New Delhi, India.

## Discussion

**Photograph 1:** Extraoral photograph of the patient showing hypertelorism, thick medial eyebrows, left side eye ptosis, flat philtrum, wide mouth, strabismus.



**Photograph 2:** Extraoral photograph of the patient showing prominent chin.



In 1965, Harry Angelman, a general paediatrician from Warrington, Cheshire, England reported three children with a similar pattern of mental retardation, seizures, ataxia, easily provoked laughter, absent speech, and dysmorphic facial features. He called them 'puppet children'. In subsequent reports by other authors, this name was altered to 'happy puppet syndrome' and this term continued in popular use for many years. It is, however, considered derogatory by the majority of parents and many professionals and the name 'Angelman syndrome' (AS) is now the preferred one.<sup>3</sup>

Williams and Fries, who have documented the natural history of this disorder.<sup>4</sup>

In the first 20 years after its description, Angelman syndrome was reported only rarely. Over the last 5 years, however, the phenotype has been more widely reported owing to both increasing interest in the cytogenetic and molecular genetic abnormalities on chromosome 15 and to the report by Boyd et al of the characteristic EEG findings in this condition. This has led to an increase in the number of Angelman syndrome patients diagnosed and to diagnosis at a younger age. The incidence of Angelman syndrome is estimated to be around 1 in 20 000 world wide.<sup>3</sup>

**Photograph 3:** Intraoral photograph of the patient showing palatally placed 14, labially placed 15, high arched palate.



**Photograph 4:** Intraoral photograph of patient showing root stump irt 46.



Angelman syndrome is a genetically- determined developmental disorder caused by deletion of the maternally inherited chromosome 15q11-13 (75% of cases) paternal uniparental chromosome 15 disomy (2-3% of cases), methylation imprinting mutation (2-3% of cases), and a *UBE3A* mutation (2-3% of cases) In the remaining 15-20% of patients, the genetic mechanism is still unknown. DNA methylation testing is a reliable screening test for deletions, uniparental disomy (UPD) or imprinting center (IC) defects, but it does not distinguish which of the three mechanisms is operative.<sup>5</sup>

A consensus for diagnostic criteria was established in 1995, and updated in 2005 by Williams et al. They appear indicative in clinical practice even if the diagnosis cannot be excluded when they are not uniformly present. Severe speech deficit, severe mental retardation, behavioral abnormalities and movement problems are ubiquitous in AS, while other features such as microcephaly or seizures may be absent. The diagnosis of AS is primarily clinical and can be confirmed by laboratory tests like Cytogenetic analysis and Fluorescent in situ hybridization (FISH) technique.<sup>5</sup>

The primary features present in our case were developmental delay, speech impairment, behavioral abnormalities, minimal movement or balance disorder, relative microcephaly, attraction to or fascination with water, wide mouth, hyperactive lower extremity deep tendon reflexes, increased sensitivity to heat, strabismus, and prognathism. All the above features are similar to the diagnostic criteria of Williams et al 2005.<sup>5</sup> The unique features present in our case are thick medial eyebrows, hypertelorism, upslant eyes with left side ptosis, bilateral cup shaped ears, flat philtrum, and narrow high arched palate.

A study was conducted by Kara B et al, at Medical Genetics department of Istanbul Medical faculty between 1995-2005. Diagnosis of Angelman Syndrome was confirmed in 14 cases, 8 female and 6 male, by the use of FISH technique. The patient age at the time of diagnosis ranged from 2- to 12 years, all patient showed developmental delay, severe speech deficit, movement and gait problem and behavioral abnormalities. 6 of them could not walk. All patient had seizures, and were on anti epileptic drugs.<sup>5</sup>

Thompson RJ, Bolton PF, reported a case in 15-year old child who was diagnosed as Angelman Syndrome at Autism Research Center, Section of Developmental Psychiatry, University of Cambridge in 2002, There was significant delay in development of both motor and language skills. He started using single words at the age of 78 months; his gait was wide based but not noticeably ataxic. He had short attention span with good physical activity. The happy demeanor with frequent laughter characteristics of Angelman Syndrome was absolute.<sup>6</sup>

Smith A et al, conducted a study of 27 Angelman Syndrome patients in Australasian, at the Department of genetics children's hospital Sydney, Australia between 1991-1994, which included 18 female and 9 male, the age of diagnosis

was between 1.5-32 years. All the patients were mentally retarded and had ataxic movements involving upper and lower limbs. Up to 6 single words were reported in 5 children's. Developmental milestones were delayed in all the children's, epilepsy was seen in 26 out of 27 patients, and EEG performed on 25 patients was recorded as abnormal.<sup>7</sup>

A study conducted by Bower BD, Jeavons PM, at University of children's hospital Birmingham in 1966, involved 2 children's diagnosed as Angelman Syndrome. The clinical features were severe mental abnormality, infantile spasm, prolonged laughter, ataxic jerky movements, prognathism, facial and ocular features and EEG abnormalities.<sup>8</sup> Similar findings were also observed in a study conducted by Robb SA, Pohl KRE, Baraister M, Wilson J, Brept EM at department of neurology and genetics in London in 1981, included 36 children with typical features of Angelman Syndrome.<sup>9</sup> Differential diagnosis of Angelman syndrome include, Rett syndrome, Mowat-Wilson syndrome, X-linked alpha-thalassemia/mental retardation syndrome (ATR-X), Phelan-McDermid syndrome.

Similar features of Angelman Syndrome and Rett Syndrome include: ataxia; brachycephaly; seizures and abnormal EEG; frequent laughter; stereotypic hand movements; and absent speech; scoliosis. The clinical differential diagnosis of Angelman Syndrome and Rett Syndrome is similar, except the presence of vasomotor instability, tremor, anxiety, absence of happy disposition, which is present only in Rett syndrome.<sup>10</sup>

Mowat-Wilson syndrome is caused by heterozygous gene on 2q22. The facial features, severe mental retardation, microcephaly, seizures and short stature resemble the Angelman Syndrome.<sup>1</sup> The differential diagnosis can be carried out on the basis of facial phenotype and confirmed by mutational analysis of the ZEB2 gene. Further molecular studies showed a deletion of the 2q22-q23 region encompassing the ZEB2 gene.<sup>11</sup>

X-linked alpha-thalassemia /mental retardation syndrome (ATR-X) is caused by mutations in the XNP gene on Xq13. These patients have severe mental retardation, there is no speech development and seizures are common.<sup>1</sup> There is Phenotypic overlap with Angelman syndrome i.e, profound mental retardation with absent speech and walking, seizures, happy disposition, emotional lability. The gene Diagnostic testing or mutational analysis allow these conditions to be excluded in most cases.<sup>12</sup>

The 22q13 deletion syndrome (Phelan-McDermid syndrome) with variable sizes of the deletion are often submicroscopic and requires special molecular cytogenetic methods to detect the deletion. Patients having developmental delay, moderate to profound mental retardation, delay of speech development and mild dysmorphic features.<sup>1</sup> Features common to Angelman syndrome and Phelan-McDermid syndrome include global developmental delay, absent speech, ataxic gait, and minor dysmorphic features. Testing for deletion 22q13 should be considered.<sup>13</sup>

There are four major genetic mechanisms which are now known to cause Angelman syndrome and AS patients have been divided into classes I to IV based on these mechanisms. A further group of patients, designated class V, have clinical features of AS but no demonstrable cytogenetic or molecular abnormality of chromosome 15q11-13. The commonest genetic mechanism giving rise to Angelman syndrome, occurring in approximately 70-75% of patients, is an interstitial deletion of chromosome 15q11-13 (Class I).

The common deletion can be detected by FISH analysis and by methylation analysis of SNRPN locus. A second class of AS patients, Class II have uniparental disomy (UPD) for chromosome 15 and thereby fail to inherit a maternal copy of UBE3A. The occurrence of UPD is sporadic and accounts for only 2-3% of cases of AS. Diagnosis is based on restriction fragment length polymorphism analysis and methylation analysis. Class III patients are those without deletions or UPD, but with abnormal chromosome 15 methylation, signifying a defect in imprinting. Imprinting defects accounts for 3-5% of patients with AS. Around 50% of subjects with imprinting defects have an identifiable mutation within the imprinting centre, but in the remaining patients no mutation can be identified and diagnosis is based on abnormal methylation analysis. Class IV patients are those who have been shown to have mutations within the gene encoding ubiquitin protein ligase, of UBE3A. These patients have normal methylation analysis and diagnosis is solely based on screening of UBE3A mutations.

Mutations can be identified in 20% of sporadic patients with normal methylation and in around 70% of familial patients. There remain some patients with clinical phenotype of AS where no chromosome 15 abnormality has been identified and these are designated as Class V patients. This accounts for about 12-15% of patients with AS. Although some would argue that these patients must have alternative diagnosis, groups with significant clinical experience of AS, suggests that class V patients do exist.<sup>14</sup> To conclude, Dentists may be confronted with rare syndrome like Angelman syndrome, which may pose challenges with the dental management.

## Reference

1. Buggenhout GV, Fryns JP. Angelman Syndrome (AS MIM 105830). *European Journal of Human Genetics* 2009; 1-7
2. <http://www.orpha.net/data/patho/GB/uk-Angelman.pdf>
3. Smith CJ, Pembrey ME. Angelman Syndrome. *J. Med Genet* 1992; 29: 412-415
4. Smiths S. Recognizable patterns of Human Malformations.— Pp 200
5. Kara B et al. Angelman syndrome: clinical findings and follow-up data of 14 patients. *The Turkish Journal of Pediatrics* 2008; 50:137- 142.
6. Thompson RJ, Bolton PF. Case Report: Angelman Syndrome in an Individual with a Small SMC(15) and Paternal Uniparental Disomy: A Case Report with Reference to the Assessment of Cognitive Functioning and Autistic Symptomatology. *Journal of Autism and Developmental Disorders* April 2003; 33(2):
7. Smith A et al. Clinical features in 27 patients with Angelman syndrome resulting from DNA deletion. *Journal of Med Genet* 1996; 33:107-112
8. Bower BD, Jeavons PM. The 'Happy Puppet' Syndrome. *Arch. Dis. Childh.* 1967; 42: 298.
9. Robb SA, Pohl KRE, Baraister M, Wilson J, Brept EM. The 'happy puppet' syndrome of Angelman: review of the clinical features. *Archives of Disease in Childhood* 1989; 64: 83-86
10. Budisteanu M et al. Phenotypic variability in Angelman syndrome- report of two cases. *A Journal of Clinical Medicine* 2008; 3(3): 192-- 197
11. Garavelli L, Mainardi PC . Mowat-Wilson syndrome. *Orphanet Journal of Rare Diseases* 2007, 2:42
12. Gibbons R. Review Alpha thalassaemia-mental retardation, X linked. *Orphanet Journal of Rare Diseases* 2006, 1:15.
13. Phelan M C. Review Deletion 22q13.3 syndrome. *Orphanet Journal of Rare Diseases* 2008, 3:14.
14. Clayton-Smith J, Laan L. Angelman syndrome: a review of the clinical and genetic aspects. *J Med Genet.* 2003 Feb; 40(2): 87-95.

# Fetal hemoglobin & liver dysfunction in sickle cell crisis

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## Abstract

Fetal hemoglobin is one of the major factors that alters the clinical course of disease. A study of 45 patients of sickle cell crisis was carried out in Department of Biochemistry & Department of Pediatrics, Pt JNM Medical College, Raipur, Chhattisgarh between June 2007 to July 2009. All patients had homozygous sickle cell anemia admitted in our institutional hospital for sickle cell crisis. Patients were diagnosed by cellulose acetate electrophoresis and adult, fetal and sickle hemoglobin was quantitated by cation exchange HPLC (Biorad Variant hemoglobin testing system). The patients were divided into three groups based on the Hb F concentration in whole blood. Group I, II and III had <10, 10-20 & >20 percent HbF respectively. HbF is higher in lesser age group but it was not statistically significant. The average Sickle cell crisis per year and recurrent events were 2.7, 3.2 and 1.4 in group-I, group-II and group-III respectively. So in group-III the crisis/year was less than compared to other two groups. The average number of blood transfusions in groups I, II & III till the study period was 14, 7.1 and 3.1 respectively. So there was a downward trend of no. of B.T with increasing level of HbF. There was significant drop in the requirement of B.T, recurrence of sickle cell crisis in the patients above HbF level of 20%. The mean size in centimeters of spleen was lower with increasing HbF level. but there was no significant difference in liver size. SGOT & SGPT was in normal reference range in patients with HbF level > 20% whereas it was abnormal in patients with HbF levels < 20%. There was no significant difference in hematological parameters like Hb, MCV, HCT, RBC, MCH & MCHC between any of the groups. However platelet count was elevated with HbF levels < 20% and in normal range with HbF levels > 20%.

## Introduction

The clinical course of sickle cell disease is variable ranging from mild clinical features to painful crisis and other complications. Fetal hemoglobin is one of the major factors

that alters the clinical course of disease. Sickle cell disease is common in tribal populations of central and southern parts of India (Kar et al, 1986 & Bhatia HM et al, 1986). Studies have shown that high HbF levels are associated with milder disease (Jackson JF et al, 1961 & Sergeant GR, 1975). Kar et al, 1986 & Perrine et al, 1978 have noted benign disease where HbF levels are high. LFT (liver function tests) were found to be normal in sickle cell disease (Richard S et al, 2002). In the present study we have tried to find correlation, if any, between HbF, liver dysfunction & clinical severity of sickle cell crisis patients.

## Material and methods

All patients were diagnosed by cellulose acetate electrophoresis and adult, fetal and sickle hemoglobin was quantitated by cation exchange HPLC (Biorad Variant hemoglobin testing system). Various hematological parameters were also measured using cell counter (xyz). Liver function tests and kidney function tests were conducted on auto-analyzer (Instrumentation laboratory model 650-I). Structured clinical details were also undertaken. Statistical analysis was done by software of Microsoft excel and statcalc.

## Results

The patients were divided into three groups based on the Hb F concentration in whole blood. Group I, II and III had <10, 10-20 & >20 percent HbF respectively.

The average Sickle cell crisis per year and recurrent events were 2.7, 3.2 and 1.4 in group-I, group-II and group-III respectively. So in group-III the crisis/year was less than compared to other two groups.

The average number of blood transfusions in groups I, II & III till the study period was 14, 7.1 and 3.1 respectively. So there was a downward trend of no. of B.T with increasing level of HbF. There was significant drop in the requirement of B.T, recurrence of sickle cell crisis in the patients above HbF level of 20%.

All patients in sickle cell crisis had splenomegaly except one who had undergone splenectomy. The mean size in centimeters of spleen was lower with increasing HbF level. but there was no significant difference in liver size.

SGOT & SGPT was in normal reference range in patients with HbF level > 20% whereas it was abnormal in patients with HbF levels < 20%. Though there was no significant difference in alkaline phosphatase level in any of groups.

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There was no significant difference in hematological parameters like Hb, MCV, HCT, RBC, MCH & MCHC between any of the groups. However platelet count was elevated with HbF levels < 20% and in normal range with HbF levels > 20%.

As evident from **table 1** HbF is higher in lesser age group but it was not statistically significant. All other parameters are not showing any alterations on comparing between three groups except the red cell diametric width which is increased in group I but it is also not statistically significant. 2 ml venous blood samples were collected in EDTA containing vial and laboratory analysis (hematological, electrophoresis and HPLC) was carried out on the same day. Another 2 ml venous blood samples were collected in plain vial, serum was separated by centrifugation, LFT and KFT was also done on the same day.

Mean levels of urea and creatinine were 28.2 mg% and 0.9 mg% in the study population which are well within normal range.

A study of 45 patients of sickle cell crisis was carried out in Department of Biochemistry & Department of Pediatrics, Pt JNM Medical College, Raipur, Chhattisgarh between June 2007 to July 2009. All patients had homozygous sickle cell anemia admitted in our institutional hospital for sickle cell crisis. Those sickle cell crisis patients who had received any blood transfusion during the last three months were excluded from the study. There were 18 females and 27

males. Average age in females and males was 9.1 years and 7.2 respectively. The patients clinical, biochemical and hematological findings were studied in correlation with fetal hemoglobin levels.

Group I, II and III had 11, 19, and 15 patients respectively. Patients were admitted for vasoocclusive crisis (26 patients), hemolytic crisis (31 patients), CNS crisis (1 patient) and acute chest syndrome (3 patients). There were 18 patients who had both hemolytic and vasoocclusive crisis. There was no mortality during hospitalization.

## Discussion

Experimental evidences indicates low levels of HbF in irreversibly sickled cells (Bertles & Milner, 1968). In vitro, HbF interferes with polymerization of sickle hemoglobin (Bertles JF et al, 1970). In vivo also HbF favorably influences biochemical and clinical events in sickle cell anemia. HbF is a risk factor for painful crisis and acute chest syndrome (Bailey K, 1992). Powars DR et al, 1984 have concluded that there may be a threshold above which HbF is effective in ameliorating the morbidity of disease. On the contrary Baum KF et al, 1987 finds no protective effect of HbF on sickle cell crisis and an earlier study by Powars DR et al, 1980 found no association between severity of sickle cell anemia and levels of fetal hemoglobin or hematological indices. Kadam et al, 1996 have reported a downward trend in painful crisis, infection, blood transfusion and

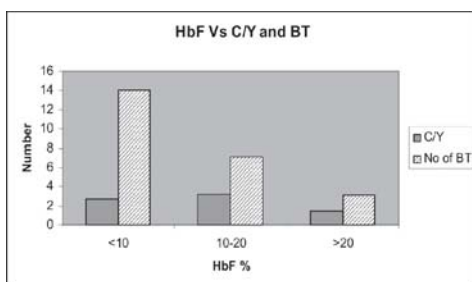
**Table 1:** Correlation of HbF with various hematological parameters

Group	HbF %		N	Age	Hb	WBC	MCV	MCHC	HCT	MCH	RBC Count	RDW
I	<10	Mean	11	9.09	5.5	14.8	78.2	34.4	20.9	26.7	3.24	23.0
		SD ±			2.7	7.3	10.3	1.8	7.5	2.6	4.2	15.9
II	10-20	Mean	19	8.1	7.4	17.3	80.9	33.2	22.2	27.0	2.8	22.7
		SD ±			1.9	8.5	9.9	3.6	6.1	4.0	0.9	14.1
III	>20	Mean	15	7	6.3	13.8	80.62	32.8	20.6	26.2	2.5	19.2
		SD ±			2.0	7.2	6.7	4.1	8.1	3.2	0.9	12.6

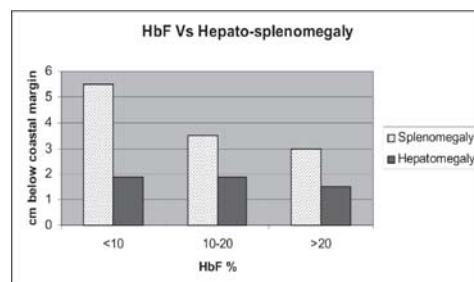
**Table 2:** Correlation of HbF with various clinical and biochemical parameters

HbF %	N	C/Y	NBT	Spleno-megaly	Hepato-megaly	Serum Bil(t)	SGOT	SGPT	ALP	Platelet count
<10	11	2.7	14	5.5	1.9	2.4	88	67	115	286
10-20	19	3.2	7.1	3.5	1.9	6.4	163	119	169	317
>20	15	1.4	3.1	3	1.5	4.6	50	38	161	200

**Figure 1:** HbF Vs C/Y and BT

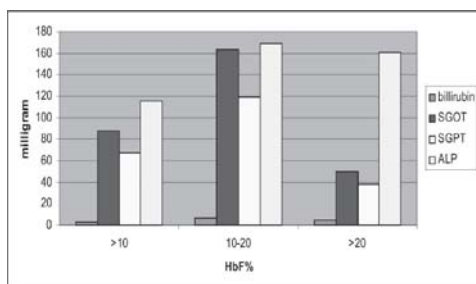


**Figure 2:** HbF Vs Hepatosplenomegaly





**Figure 3: HbF Vs LFT**



hospitalization with increase in HbF level.

In the present study we found that HbF level did not had any significant effect on painful crisis, recurrent events, blood transfusion, hospitalization & number of crisis when HbF level was less than 20% but when HbF level was higher than 20% it favorably influenced painful crisis, recurrent events, blood transfusion, hospitalization & number of crisis. Powars DR et al have also suggested that HbF level below 15% had no significant difference in crisis, but HbF level more than 20% had low incidence of CNS crisis, acute chest syndrome and recurrent painful events. In another study Alabdabali MK et al, 2007 also found that African patients frequently suffers from acute chest syndrome with more I.C.U. stay than patients of eastern province of Saudi Arabia because of more HbF level in patients of Saudi Arabia.

All patients in our study had splenomegaly except one who had undergone splenectomy. We observed persistence of splenomegaly at any levels of HbF, but there was a downward trend in the size of spleen below coastal cartilage as HbF level goes up (figure 2). Serjeant GR, 1970 & Kadam et al, 1996 have also reported persistence of splenomegaly with higher HbF level but they haven't mentioned the size of spleen. This might indicate that size of spleen could be a rough guide to the clinical severity of disease in sickle cell crisis patients.

We observed SGOT, SGPT & platelet levels to be higher with low levels of HbF levels and which normalized with elevated HbF level. Richards et al, 2002 have also reported increase in AST during Vasoocclusive crisis state than steady state of sickle cell anemia.

In the present study patients with elevated HbF levels had less severity of crisis & less altered liver enzymes as compared to patients with low level of HbF who had more severe crisis & elevated levels of hepatic enzymes.

Our study does not show any alteration in hematological parameters in different groups. But Donaldson et al in 2001 have reported that there was a positive trend between HbF grouping and Hb, PCV, MCH.

## Conclusion

HbF influences clinical severity of sickle cell crisis. When HbF level is higher than 20% it reduces in painful crisis, recurrent events, blood transfusion, hospitalization &

number of crisis. The size of enlarged spleen also correlates with HbF level so it could be a valuable clinical feature in assessing the severity of sickle cell crisis in resource limited areas. SGOT, SGPT & platelet count needs to be monitored in crisis patients as they well correlate with HbF levels.

## Acknowledgement

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## Conflict of interest statement

We declare that we have no proprietary, financial, professional or other personal interest of any nature or kind in any product, services/company that could be construed as influencing the position presented in, or the review of, the manuscript entitled 'FETAL HEMOGLOBIN & LIVER DYSFUNCTION IN SICKLE CELL CRISIS'

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## Reference

- Alabulaali MK. Sickle cell disease patients in eastern province of Saudi Arabia suffer less severe acute chest syndrome than patients with African haplotypes. *Annals of Thoracic Medicine* 2007;Vol 2 Issue 4:158-162.
- Bailey K, Morris JS, Thomas P & Serjeant GR. Fetal hemoglobin and early manifestations of homozygous sickle cell disease. *Archives of Diseases in Childhood* 1992;67:517-520.
- Baum KF, Dunn DT, Maude GH & Sergeant GR. The painful crisis of homozygous sickle cell disease: a study of risk factors. *Archives of internal medicine* 1987;147:1231-1234
- Bertles JF, Rabinowitz JFR & Dobler J. Hemoglobin interaction: modification of solid phase composition in the sickling phenomenon. *Science* 1970;169:375-377.
- Bertles JF & Milner PF. Irreversibly sickled erythrocytes: a consequence of heterogenous distribution of hemoglobin types in sickle cell anemia. *Journal of Clinical Investigation* 1992;47:1731.
- Bhatia HM, Rao VR. Genetic atlas of the Indian tribes. Published in 1986 by Institute of immunohaematology, ICMR, Bombay, India.
- Darleen R Powars, Joyce N Weiss, Linda S Chan & WA Schroeder. Is there a threshold level of fetal hemoglobin that ameliorates morbidity in sickle cell anemia?. *Blood* 1984;Vol. 63 No. 4: 921-926.



- Donaldson A, Thomas P, Serjeant BE, Serjeant GR. Fetal hemoglobin in homozygous sickle cell disease: a study of patients with low HbF levels. Clin Lab Haem 2001;23:285-289.
- Jackson JF, Odom JL & Bell WN. Amelioration of sickle cell disease by persistent fetal hemoglobin. Journal of American Medical Association 1961;177:867-869.
- Powars DR, Schroeder WA, Weiss JN. Lack of influence of fetal hemoglobin levels or erythrocyte indices on the severity of sickle cell anemia. J Clin. Invest. 1980;65:732-740.
- Kadam MD, Mukherjee MB, Colah RB, Gangakhedkar RR, Mohanty D. Is fetal hemoglobin level a prognostic indicator for severity of sickle cell disease?. Ind. J Hum. Genet. 1996;2:43-49.
- Kar BC, Satapathy RK, Kulozik AE et al. Sickle cell disease in state of Orissa state, India. The Lancet 1986;Nov. 22:1198-1201.
- Perrine RP, Pembrey ME, John P, Perrine S & Shoup F. Natural history of sickle cell anemia in Saudi Arabia. Annals of internal Medicine 1978;88:1-6.
- Richard S, Billet HH. Liver function tests in sickle cell disease. Clin. Lab. Haem. 2002;24:21-27.
- Serjeant GR. Irreversibly sickled cells and splenomegaly in sickle cell anemia. British Journal of Hematology 1970;19:635-641.
- Sergeant GR. Fetal hemoglobin in homozygous sickle cell disease. Clinical hematology 1975;4:109-122.

# Root supported overdenture using Zest Anchor locator attachment-a case report

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## Abstract

Root-supported overdentures are an alternative to extractions and complete dentures. Chewing efficiency with a root-supported overdenture is higher in patients who previously wore a complete denture. This increases in function, retention, and stability leads to better esthetics and phonetics in denture wearers, thereby elevating patient's self-esteem. This article demonstrates a technique of fabrication of root supported overdenture, using Locator attachments (Zest Anchors, Inc.) to provide retention and stability and resistance to denture displacement. Locators can be used to attach to roots with or without a coping in a direct or indirect technique. Retaining the existing teeth also preserves the alveolar bone and increases both proprioception and masticatory performance.

## Keywords

Root supported overdenture, Locator attachment, Preservation of alveolar bone.

## Introduction

The preservation and use of remaining roots as the foundation for an overdenture has been in use as a cost-effective treatment modality for over a century. Root-supported overdentures can solve the problems created by the edentulous mandible and maxilla – preserving the alveolar ridge, masticatory function and preventing bone loss while increasing denture retention, stability and resistance to displacement. At the same time, the soft tissue of the residual ridge receives less abuse as the abutment teeth share support. Natural teeth that are unacceptable for conventional dental use are acceptable for tooth-supported dentures (and as the root-crown ratio is improved by reducing the occlusal height of the tooth down to the level of the tissue surrounding it, the prognosis for these teeth becomes far more favourable). Patients also enjoy the proprioception, the awareness of jaw-space relationships that is impaired, if not lost entirely, when teeth are extracted along with improved biting force and neuromuscular control.

This article demonstrates a technique of fabrication of root supported overdenture, using Locator attachments (Zest Anchors, Inc.) to provide retention and stability and preserving the remaining alveolar bone. Locators can be used to attach to roots with or without a coping in a direct

or indirect technique. This case will demonstrate their use in a direct technique without a coping.

## Case report

A 45 year old male patient reported to the outpatient post graduate department of Prosthodontics, Sardar Patel Post Graduate Institute of dental and Medical Sciences, Lucknow, with the chief complaint of difficulty in eating food and trauma to the upper gums by the lower teeth. Intra oral examination (Fig.1a) revealed the presence of both maxillary cuspids and a complete set of mandibular teeth. The panoramic radiograph (Fig.1b) showed an adequate amount of bone support in relation to both the maxillary canines. Two treatment plans were proposed to the patient; plan a- Extraction of both maxillary canines and fabrication of single complete maxillary denture, plan b- Fabrication of maxillary complete overdenture using attachments. Since the patient expressed a strong desire to preserve his teeth and avoid surgery, fabrication of overdenture was planned.

First, a thorough oral prophylaxis was done followed by endodontic treatment of the maxillary canines. Then, the coronal portion of both the canines was reduced to the gingival level and a thin chamfer finish margin was prepared on the remaining portion of the abutment. (Fig.2) This was followed by the fabrication of the maxillary overdenture using conventional technique.

## Root preparation

The next step was to prepare the root to receive the Locator post. The Locator Root Attachment Kit (Zest Anchors, Inc) (Figure 3) contains a post bur to prepare the canal space of the same size as that of the female post. At least 5 mm of gutta-percha was left as an apical seal. A diamond bur was then used to create an internal dentinal seat for the Locator female post (If needed, 10°- or 20°-angle correction posts may be used to correct divergent roots. It is recommended by the manufacturer to parallel the path of insertion of the Locator attachments for root form prosthesis to less than 10° of divergence.)<sup>1</sup>

The parallelism of the locator post was checked using the black coloured plastic alignment rods (Fig.4). Then the locator post was luted in the canal post space using type I luting GIC cement. (Fig.5a&b)

The metal housings (Fig.6) containing the male nylon processing components were then placed onto the posts

cemented into the cuspid roots. The intaglio surface of the denture was hollowed out in the cuspid areas to allow complete intraoral seating of the denture without interference from the bulk of the two housings. A small relief hole was made in the denture to allow for extrusion of excess resin.

A thin layer of self cure resin was applied to the denture in the hollowed out area. The housings, which included white spacer rings (Fig.7), were returned to the Locator females. A direct pick-up of the housings in the denture was accomplished (Fig.8). After the denture was adjusted and polished, the occlusion was verified. The Locator Tool was then used to remove both nylon processing components from the metal housings incorporated in the denture. Retentive nylon male (Fig.9) components of various color coded retentions can then be placed as dictated by the needs of the patient. After the rehabilitation of the maxillary canines, the patient was instructed in the proper care of his root attachments by using a daily fluoride gel and performing meticulous plaque control. Regular recall appointments were scheduled to check for patient compliance and appropriate tissue fit of the denture.

(Fig.10)

## Discussion

Root-supported overdentures gain their retention and stability from the use of attachments. Attachments are simple connectors consisting of two or more parts. One part connects to the root and the other part to the overdenture acrylic denture base. Attachments are either resilient or nonresilient (rigid).

There are three types of overdenture attachment designs: *bar type, supra radicular type, and intraradicular type*. The bar type spans an edentulous area and connects two or more teeth or implants with rigid fixation. Supraradicular type attachments are placed on top of the existing root structure or surgically placed implants. Intraradicular attachments are placed within the endodontically treated root structure of natural teeth or implants. All three designs are used in the construction of maxillary and mandibular overdentures <sup>2, 3, 4</sup>.

The Locator root-retained attachment (Zest Anchors, Escondido, CA: (800) 262-2310) is classified as a

**Figure 1.a.** Pre operative photograph.



**Fig 2.** Decoronated cuspids.



**Fig 4.** Black coloured plastic alignment rods (To check parallelism).



**Fig 1b.** OPG X-RAY.



**Fig 3.** Locator attachment kit.



**Fig 5.a.** Cuspids with luted female posts.



**Fig 5b.** IOPA X-Ray showing 13 and 23 with female post.



**Fig 7.** Cuspids with white block out spacer



**Fig 9.** Retentive nylon male component.



**Fig 6.** Canine with metal housing



**Fig 8.** Denture with metal housing.



**Fig 10.** Post operative Photograph.



supraradicular, universal hinge, resilient attachment for endodontically treated roots. It is indicated for use with overdentures or partial dentures, retained in whole or in part by endodontically treated roots in the mandible or maxilla. It is contraindicated where a totally rigid connection is required. The supraradicular attachments (self-locating design) allow patients to seat their overdenture easily without the need for accurate alignment of the attachment components. It is designed with a locating skirt that seats the attachment in the proper location every time, regardless of the patient's ability or dexterity. It is ideal for stroke patients or arthritis patients who have compromised dexterity and difficulty in exact overdenture placement. The pivoting Locator male, allows a resilient connection for the prosthesis. The retentive nylon male remains completely in contact with the female socket while the metal denture caps have a full range of rotational movement over the male. The unique dual retention, (both inside and outside), provides the Locator attachment with a greater retention surface area than other attachments.<sup>5</sup>

Vygandas Rutkunas, Hiroshi Mizutani evaluated the

retentive and stabilizing properties of stud (ERA Overdenture (orange and white), Locator Root (pink) and OP anchor # 4) and magnetic attachments (Hyperslim 4513, Hyperslim 4013, Magfit EX600W, Magnedisc 500 and Magfit-RK) in retaining mandibular overdenture. They found that the Stud attachments provide stronger retentive and stabilizing forces than magnetic attachments with all types of dislodgements.<sup>6</sup>

Diagnosis and treatment planning are most important for the success of overdentures. Evaluation of the existing limited abutments- for endodontic and periodontal treatment is the first step in a successful treatment plan. Teeth with advanced periodontitis having less than 6.0 mm of bone support, subgingival decay, and poor attached gingival tissue are contraindicated for overdentures<sup>7</sup>. Overdentures require particularly careful assessment of vertical space. There must be sufficient room for roots, copings, and possible attachments, together with an adequate thickness of denture base material and artificial teeth, all this without jeopardizing the strength of the denture.<sup>8</sup>

Performing endodontic therapy on overdenture abutment

teeth accomplishes a number of objectives, including retaining the natural tooth root in its alveolar bony environment for retention, support, and stability of the overdenture, preserving and maintaining the height of the alveolar bone and ridge: maintaining the proprioceptive quality and integrity of the periodontal ligament: and creating a favourable crown-to-root ratio for periodontally involved abutment teeth.<sup>9,10</sup>

Overdentures also help in improving the masticatory efficiency in edentulous patients. Rissin and House analyzed the masticatory performance of three dental patient groups: those with natural dentition, those wearing complete dentures, and those wearing overdentures. Food was chewed by each patient, and then passed through a No. 12 sieve. The chewing efficiency of patients with natural dentition was measured at 90%, complete denture wearers 59%, and patients with overdentures 79%.<sup>11</sup>

Delsen Testing Laboratories<sup>12</sup>, Inc. performed an insertion and extraction test of retention loss.<sup>20</sup> The Locator attachment did not wear out until 110,000 cycles were completed. The ZAAG attachment wore out in 12,000 cycles and the ERA in 4,000 cycles. This new Locator attachment creates a longer lasting, more retentive attachment for root-supported and implant-support overdentures.

The role of dental auxiliaries in the maintenance of overdentures is very important. Most candidates for full dentures or overdentures may not be in a daily habit of brushing and oral cleansing. Overdenture attachments must be kept clean and free from plaque and food debris. Daily brushing and placement of the overdenture in an antibacterial solution are most important. In patients with root-supported overdentures, it is recommended by many dentists that overdenture abutments should be brushed at least once a day with gel toothpaste to remove plaque and to stimulate gingival tissues. A daily application of 1.1% neutral sodium fluoride is also recommended.

### Summary and conclusions

To grow as people and to increase our knowledge as dentists, we must reach out to new ideas, solutions, and techniques. The root-supported overdenture is one solution to the problem presented by an edentulous maxilla and mandible. Careful diagnosis and treatment planning are important for the success of overdentures. This alternative treatment to extraction of natural teeth and complete dentures provides the patient with greater

retention, stability, and comfort and improved function, esthetics, and phonetics. The Locator attachment is designed for patients who have difficulty seating their overdentures. Stroke and arthritis patients are ideal candidates for this attachment. The technique for constructing root-supported overdentures is easily within the skill level of most general dentist.

A case of rehabilitation of an edentulous maxillary arch with retained canine, used as overdenture abutments and locator attachments (Zest Anchor™) has been presented.

### References

1. Allen L. Schneider, And William A. Lobel, Attachment Adaptation To An Existing Maxillary Overdenture . Inside Dentistry article Reprint Vol. 4 No. 2, 2008
2. Pavlatos J. Root-supported overdentures. CDS Rev 1998;9 1:20-25
3. Sterngold/Implamed. Procedure manual. Sterngold;1998:3.1-4
4. Staubli P. Attachments and implants reference manual, ed. 6. San Mateo, CA: Attachments International; 1999:1-9.
5. James Pavlatos, DDS Reprinted from General Dentistry September/ October 2002.
6. Vygandas Rutkunas, Hiroshi Mizutani Retentive And Stabilizing Properties Of Stud And Magnetic Attachments Retaining Mandibular Overdenture. An In Vitro Study Stomatologija, Baltic Dental and Maxillofacial Journal, 6:85-90, 2004
7. Morrow RM. Handbook of immediate overdentures. St. Louis: Mosby;1978:48.
8. Del Rio CE, Fielden JE, Grandich RA. Clinical appointment. III. Endodontics. In: Handbook of immediate overdentures. St. Louis: Mosby;1978:48
9. Castleberry DJ. Philosophies and principles of removable partial overdentures. Dent Clin North Am 1990;34:589-592.
10. Renner RP. The overdenture concept. Dent Clin North Am 1990;34:593-606.
11. Rissin L, House JE, Manly RS, Kapur KK. Clinical comparison of masticatory performance and electromyographic activity of patients with complete dentures, overdenture, and natural teeth. J Prosthet Dent 1978;39:508-511.
12. Delsen Testing Laboratories, Inc. Insertion and extraction test of retention loss: Test report 3-30-2000;1-7.

# Geographic information system in analysis and evaluation of Swine flu

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## Abstract

Swine flu (swine influenza) is a respiratory disease caused by viruses (influenza viruses) that infect the respiratory tract of pigs and result in nasal secretions, a barking-like cough, decreased appetite, and listless behavior. Swine flu produces most of the same symptoms in pigs as human flu produces in people. Global outbreak of a new strain of influenza A virus subtype H1N1, officially named the "new H1N1", first identified in April 2009, and commonly called "Swine flu" is not caused by a swine influenza virus only. Their cause is a new strain of virus of influenza A H1N1 that contains genetic material matched a strain of human influenza virus, a strain of avian influenza virus, and two separate strains of swine influenza virus. The origins of this new strain are unknown and the World Organization for Animal Health (OIE) reports that this strain has been isolated from pigs.

One of the most challenging and unexplored issues is the ability to determine the spread patterns, the ability to predict future spread patterns and the ability to evaluate the effectiveness of the methods that are used in curbing future spread patterns of H1N1. The purpose of this paper is therefore aimed at introducing the technique of Geographic Information Systems (GIS) in activities that are undertaken by organizations with special emphasis on programmes that are put in place in the fighting of Swine flu.

## Keywords

GIS, H1N1, Swine Flu, Database, Data Analysis, Management

## Introduction

The swine flu (also known as swine flu or flu pork) is an infectious disease caused by any virus belonging to the family Orthomyxoviridae, which is endemic in populations' pig [1]. These strains virus, known as swine influenza virus (SIV) have been classified into Influenza virus C or one of the subtypes of the genus Influenza virus A (being the best known strains H1N1, H3N2, H3N3, isolated in Quebec, and H1N2, isolated in Japan and Europe) [2], [3], [4].

The H1N1 is a descendant of the Spanish flu which was a pandemic disease in the 2nd decade of the 20 century during 1918-1920. After the completion of the pandemic virus persisted in pigs, and with it the descendants of the 1918 virus have circulated in humans over the course of

the twentieth century, contributing to the appearance of normal seasonal influenza annually. However, direct transmission from pigs to humans is quite rare, with only 12 cases have shown in the United States since 2005 [5], [6].

Although the swine flu does not affect regular human population, there are sporadic cases of infections in humans. Generally, these cases occur in those working with poultry and pigs, especially those individuals who are heavily exposed to this type of animal, and are at higher risk of infection if they carry any viral strain that is also capable to infect humans [7].

Global outbreak of a new strain of a influenza A virus subtype H1N1, officially named the "new H1N1", first identified in April 2009, and commonly called "Swine flu" [1] is not caused by a swine influenza virus only. Their cause is a new strain of virus of influenza A H1N1 that contains genetic material matched a strain of human influenza virus, a strain of avian influenza virus, and two separate strains of swine influenza virus. The origins of this new strain are unknown and the World Organization for Animal Health (OIE) reports that this strain has been isolated from pigs [8]. It is transmitted easily between humans, due to an ability attributed to a mutation not yet identified, and makes it through the saliva, by air, by close contact between the mucous membranes or through hand-mouth transmission due to contaminated hands [7].

Symptoms of swine flu are similar to most influenza infections: fever, cough, nasal secretions, and sore throat, muscle pains, headache, some patients also get nausea, vomiting, and diarrhea [9], [10], [11]. people at higher risk of serious complications included people age 65 years and older, children younger than 5 years old, pregnant women, and people of any age with underlying medical conditions, such as asthma, diabetes, obesity, heart disease, or a weakened immune system (e.g., taking immunosuppressive medications or infected with HIV) [10],[12].

The basic preventive methods that have been stressed upon in fighting swine flu is Keep a distance of at least 6 feet from the ill person), Personal protective equipment: fit-tested N95 respirator (if unavailable, wear a medical (surgical mask), Wash hands thoroughly with soap and water or alcohol-based hand gel.

However due to cultural, social, political and other secondary influences, these methods have not been effective up to the desired level. There is therefore a need

to explore other strategies that can be incorporated alongside the laid down strategies or any other strategy so that the effectiveness of these methods can be achieved to the desired level.

One of the most challenging and unexplored issues is the ability to determine the spread patterns, the ability to predict future spread patterns and the ability to evaluate the effectiveness of the methods that are used in curbing future spread patterns of swine flu .

The world is divided in different continents and countries. Various organizations have carried out different programmes in these regions and a GIS is automatically an important tool for integrating these programmes and carrying out comprehensive analysis of the programmes impacts. A GIS would present an integrated output that is effective in worldwide planning of intervention strategies. This paper will address its goal by identifying the significant effects of H1N1 through a scientific investigation and to demonstrate the usefulness of GIS techniques in analyzing and mapping its spatial distribution patterns.

A project designed along these lines should fulfill particular fundamental objectives. This should be demonstrated by the project's ability to;

1. Instantly show the occurrence of swine flu patterns in form of a map (digital/ hard copy) showing high risk and low risk areas.
2. Instantly determine the geographic location of areas of highest demand for intervention programmes.
3. Build questions and be able to obtain instant answers e.g. what is the pattern of occurrence of swine flu?
4. Easy and effective data manipulation

## 1. Current impacts of H1N1

The current status of the Swine Flu epidemic globally is characterized by a high rate of H1N1 infection and a growing number of illnesses and deaths among the world's citizens.

According to WHO's report (World Health Organization) On July 24, 2009, the pandemic was still in its early stages globally and two billion infections over the course of the pandemic was "a reasonable ballpark to be looking at" [13]. On the same day, the U.S. (Centers for Disease Control and Prevention) CDC's National Center for Immunization and Respiratory Diseases (on July 24, 2009), estimated that current trends suggest 12% to 24% of Americans might get swine flu this fall and winter.

In late June, the CDC estimated that 1 million Americans had so far contracted the flu. By comparison, an estimated 15 million to 60 million Americans are infected with the seasonal flu each year, leading to roughly 36,000 deaths [14]. According to the CDC, however, only about one in 20 cases was being officially reported in the U.S. in late May [9]. In the U.K., some experts thought the number of cases was potentially 300 times more than early published estimates [15], warning that case estimates by the U.K. and other governments were "meaningless" and hiding its true extent. There were also estimates that Japan may have had

approximately 30,000 cases by late May [15].

There is a growing consciousness that the millions people estimated to be currently infected with H1N1 and millions of others will become infected in the coming years, and that a set of inter-related social, economic and social crises for communities and the world will increase, unless swift and appropriate action is pursued immediately.

## 2. GIS (geographic information systems)

### 2.1. Definition

It is a systematic integration of Computer Hardware, Software and Spatial Data, for capturing, storing, displaying, updating manipulating and analyzing, in order to solve complex management problems [16].

### 2.2. How a GIS works

A GIS stores information about the world as a collection of thematic layers that can be linked together by geography. Geographic information contains either an explicit geographic reference such as a latitude and longitude or national grid coordinate, or an implicit reference such as an address, postal code, census tract name, forest stand identifier, or road name. Implicit references can be derived from explicit references using an automated process called "geocoding." These geographic references allow you to locate features and events on the surface of the earth for analysis.

Geographic information systems work with two fundamentally different types of geographic information, the "raster model" and the "vector model."

GIS is designed to produce information in support of decision making. It may be manual or computerized. The malfunctioning capabilities of a GIS make it widely applicable to any problem involving georeferenced data. Given that there are systems that can handle spatial data, database management and data analysis, the major driving force for the adoption of GIS for use in mapping, analysis and evaluation of H1N1 occurrence patterns can be viewed in terms of the following advantages over other conventional methods [17].

#### 2.2.1. Information retrieval

With a GIS one can 'point' at a location, object or area on the screen and retrieve Swine flu information about it from off-screen files. One can query a GIS about the status of the area with relation to other areas. This kind of analytical function allows one to draw conclusions about the area. It also increases the speed of working and reduces the costs.

#### 2.2.2. Topological modeling

A GIS can recognize and analyze the spatial relationships that exist within digitally stored spatial data. These topological relationships allow complex spatial modeling and analysis to be performed. Topological relationships between geometric entities traditionally include adjacency (what adjoins what), containment (what encloses what), and proximity (how close something is to something else)

[18].

### 2.2.3. Networks

If all health facilities in an area were co-ordinated or related by roads, then a GIS can determine the distance and time one can take to reach a particular health facility from his home. A GIS can simulate the shortest routes to reach certain facilities [19].

### 2.2.4. Map overlay

The combination of several spatial datasets (points, lines or polygons) creates a new output vector dataset, visually similar to stacking several maps of the same region. E.g. using maps of population and maps of infection, a GIS can produce a new map layer or overlay that ranks the regions according to infection rate.

### 2.2.5. Data output

A critical component of a GIS is its ability to produce graphics on the screen or on paper that convey the results of analysis to people who make decisions about resources. Graphical, digital and statistical information as well as maps can be generated thereby allowing the viewer to visualize and understand the results of analysis or simulations of special events.

## 3. Equipment and materials

A GIS that is designed to handle data relating to HIV or other diseases should have the following equipment and material [18];

### 1. Hardware

- HDD(*Hard Disk Drive*) – For data and software storage; data processing and manipulation; overall system control
- Digitizer – For data digitization in the vector format.
- Digital plotter – For output of hardcopy graphics.
- Printer – Report and table output.
- Tape/CD drive – offline data import; back up; external storage.
- Modem – intercomputer communication; Internet access.
- UPS – regulation of power supply

### 2. Software

Software is a set of instructions (programmes) that a computer can carry out. The GIS software refers to a geographic information system application, which is software used to create, manage, analyze and display geospatial data on digital maps [18]. Within industry, commercial offerings from companies such as Autodesk, Bentley Systems, ESRI, Intergraph, Manifold System and Smallworld dominate, offering an entire suite of tools.

When purchasing GIS software, one should be able to understand these modules and know the specifics that are required. There are many GIS software that can handle data relating to H1N1. Among these include; Arcview, Arcinfo, Arcmap, Idrisi, Ilwis etc .

### 3. Data

Data refers to the material from which information should be processed. These data can be grouped into different categories depending on available statistics e.g. [18].

- √ Number of people infected with Swine flu per area (District, province, state, country etc)
- √ Number of people who have developed Swine flu
- √ Number of people who have died as a result of Swine flu

The data can be grouped into different classes e.g. by sex (male, female), Age (Children/adults)

## 4. Methodology

An overview of the method that can be used is illustrated in the table 1.

**Table 1:** Overview of the Methodology

- |                                                                                                                                                                                                                                                                                                              |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <ol style="list-style-type: none"><li>1. Data identification and collection</li><li>2. Getting spatial data into the database</li><li>3. Getting attribute data into the database</li><li>4. Linking the database</li><li>5. Performing analysis</li><li>6. Presenting the results of the analysis</li></ol> |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

### 4.1. Data identification and collection

This refers to the identification, collection; digitization and correction of errors for the data necessary in the building of GIS database .Two types of data are used. They include [18]:

#### 4.1.1. Spatial data

Also known as geospatial data, it is the data or information that identifies the geographic location of features and boundaries on Earth, such as natural or constructed features, oceans, and more. Spatial data is usually stored as coordinates and topology.

There are two broad methods used to store spatial data in a GIS for both abstractions: Raster and Vector.

A raster data type is, any type of digital image represented in grids. Raster data type consists of rows and columns of cells, with each cell storing a single value. Raster data can be images (raster images) with each pixel (or cell) containing a color value.

In a GIS, geographical features are often expressed as vectors, by considering those features as geometrical shapes. Different geographical features are expressed by different types of geometry (Point, Polylines, and polygon).

#### 4.1.2. Non spatial / attribute data

Additional non-spatial data can also be stored along with the spatial data represented by the coordinates of vector geometry or the position of a raster cell. In vector data, the additional data contains attributes of the feature. For example, Swine flu statistics, population statistics [16]. In raster data the cell value can store attribute information, but it can also be used as an identifier that can relate to records in another table.



## 4.2. Database design and creation

To achieve the best of GIS data, the database is designed and stored in such a way that it can be easily and repeatedly be accessed by different users, and that it can satisfy most of the needs of the users.

Since the data handled is large and diverse from different sources, the database is organized in a series of tables so that it can be shared. Each table is called a relation and it consists of a number of rows and columns. Once the database has been created, then it can be managed by a DBMS (Database Management Systems).

A database has many users, each of who may have a different perspective (view) of the data. The DBMS by being able to abstract just the data needed by each user is able to provide these different user views, without presenting the whole database to each user.

## 4.3. Data Analysis

The heart of GIS is the analytical capabilities of the system. What distinguish the GIS system from other information system are its spatial analysis functions. The analysis of H1N1 database comprises of tools and operations that use the spatial and non-spatial attributes in the database to answer questions about the real world [16].

### 4.3.1. Categories of Analysis Functions

There are three broad categories.

#### 1) Database query

The selective display and retrieval of information from a database are among the fundamental requirements of GIS. The ability to selectively retrieve information from GIS is an important facility. Database query simply asks to see already stored information. Basically there are two types of query most general GIS allow: 1.Query by attribute, 2.Query by geometry.

Map features can be retrieved on the basis of attributes, For example, show areas with percentage infection of H1N1 above 10 percent, Many GIS include a sophisticated function of RDBMS known as Standard Query Language (SQL), to search a GIS database. The attribute database, in general, is stored in a table (relational database mode.) with a unique code linked to the geometric data. This database can be searched with specific characteristics. However, more complex queries can be made with the help of SQL. GIS can carry out a number of geometric queries. The simplest application, for example, is to show the attributes of displayed objects by identifying them with a graphical cursor.

#### 2) Derivative mapping

This involves the combination of selected components of the database to yield new layers that may also become additions to database .Common Derivative mapping functions include;

√ Overlay: The combination of several spatial datasets (points, lines or polygons) creates a new output vector dataset, visually similar to stacking several maps of the

same region.

- √ Proximity analysis: Proximity analysis is one way of analyzing locations of features by measuring the distance between them and other features in the area.
- √ Polygon search: it involves determining whether a given point or line lies within a given polygon.
- √ Network analysis: A network is a system of connected linear features through which resources flow e.g. road network

### 3) Modeling

Example is modeling of an unknown relationship between variables in order to use it to predict other variables [20].

### 4. Data presentation

H1N1 data can be presented in different forms depending on the capabilities of the software that is used. The forms in which the data can be presented include: 1.Digital maps, 2.Bar graphs, 3.Pie charts, 4.Line graphs.

## Conclusions and recommendations

This paper has addressed the challenge of exploring other strategies that can be used alongside the laid down strategies in fighting the epidemic. As has been seen, this can be achieved using GIS techniques through integrated analysis. The digital map can be produced which have the benefit of easier revision and spatial analysis, besides a clear representation of geographically referenced information. GIS techniques are therefore highly suitable for analysis of Swine flu occurrence patterns and planning of punctual preventive measures to mitigate it.

As it has been put forward in this paper, the use of GIS in mapping, analysis and evaluation of H1N1 occurrence patterns has greater potential of being the first step towards achieving an integrated analysis of H1N1 world wide Enough resources should be projected towards this technique and make it a reality. An expert system can be developed which among other things will be able to:

- √ Make decisions about H1N1 basing on its knowledge base
- √ Be able to give instructions from fore facts
- √ Reason and explain its procedures.

Since Swine flu is becoming a global disaster, the database created should be shared and be made available to different organizations and individuals across the world through the Internet. This should include designing of software that can enable people who are not specialists in GIS or who do not understand the GIS software to be able to access this information easily on the web.

## References

1. Virology.ws, Reassortment of the influenza virus genome. <http://www.virology.ws/2009/06/29/reassortment-of-the-influenza-virus-genome/>, 2009-06-29( Retrieved on 2009-08-13).
2. Bouvier, N.M., Palese P The biology of influenza viruses.

- Vaccine, September 2008. 4: p. 49-53.
3. Kimura, H., Abiko C, Peng G, et al Interspecies transmission of influenza C virus between humans and pigs. *Virus Research*, April 1997. 48(1): p. 71-9.
  4. Matsuzaki, Y., Sugawara K, Mizuta K, et al Antigenic and genetic characterization of influenza C viruses which caused two outbreaks in Yamagata City, Japan, in 1996 and 1998. *J. Clin. Microbiol*, February 2002. 40(2): p. 422.
  5. Knobler, S., Mack A, Mahmoud A, Lemon S, ed, 1: *The Story of Influenza". The Threat of Pandemic Influenza: Are We Ready? Workshop Summary 2005*: p. 75.
  6. Olsen, C.W., The emergence of novel swine influenza viruses in North America. *Virus Research* May 2002. 85(2): p. 199-210.
  7. Gray, G.C., Kayali G, Facing pandemic influenza threats: the importance of including poultry and swine workers in preparedness plans. *Poultry Science*, April 2009. 88(4): p. 880.
  8. Kothalawala, H., Toussaint MJ, Gruys E, An overview of swine influenza. *Vet Q*, June 2006. 28(2): p. 46-53.
  9. CDC, Briefing on Investigation of Human Cases of H1N1 Flu. <http://www.cdc.gov/media/transcripts/2009/t090724.htm>, 2009-07-24(Retrieved on 2009-07-28).
  10. CDC, What to do if you get flu-like symptoms. <http://www.cdc.gov/h1n1flu/sick.htm> 2009( Retrieved on 2009-05-22).
  11. W.H.O, About the disease. [http://www.who.int/csr/disease/swineflu/frequently\\_asked\\_questions/about\\_disease/en/index.html](http://www.who.int/csr/disease/swineflu/frequently_asked_questions/about_disease/en/index.html), 2009-05-01( Retrieved on 2009-05-22).
  12. New York Times, 'Underlying conditions' may add to flu worries. <http://www.nytimes.com/2009/05/28/health/policy/28flu.html>, 2009( Retrieved on 27 May 2009 ).
  13. CBS News, WHO: Swine Flu Could Infect 2 Billion. 2009(Retrieved on 24 June 2009).
  14. CDC, 1 Million Americans Likely Stricken by Swine Flu: CDC. *Forbes*, 2009(Retrieved on 25 June 2009).
  15. Independent, T., UK swine flu toll is really 30,000, says leading scientist. <http://www.independent.co.uk/life-style/health-and-wellbeing/health-news/uk-swine-flu-toll-is-really-30000-says-leading-scientist-1690130.html>, 2009(Retrieved on 24 May 2009).
  16. Taravat Najafabadi, A., Applications of GIS in Health Sciences. *Shiraz E-Medical Journal* 2009. 10(4): p. in press.
  17. Tanser, F., LeSueur D, the application of geographical information systems to important public health problems in Africa. *International Journal of Health Geographics* 2002. 1: p. 4-12.
  18. Longley, P., A. , Goodchild, M. F., Maguire, D. J. and Rhind, D. W., *Geographic Information Systems and Science*. 2nd ed. 2005: Wiley. 517.
  19. Ferguson, E., C., Maheswaran, R., and Daly, M., Road-traffic pollution and asthma - using modeled exposure assessment for routine public health surveillance. *International Journal of Health Geographics* 2004. 3(24).
  20. Carrat, F., Valleron, A.J., Epidemiologic mapping using the kriging method: application to an influenza-like illness epidemic in France. *Am. J. Epidemiol*, 1992. 135: p. 1293-1300.

# Lack of tolerance observed to hypnosedative actions upon repeated treatment with the novel hypnosedative Zopiclone (Cyclopyrrolone) in animal models for hypnosedation

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## Abstract

### Background

Benzodiazepine (BZD) hypnosedatives are widely used for treatment of insomnia and anxiety, since last 5-6 decades. Large number of BZD analogues has been synthesized to obtain superior risk/benefit ratio since then. Most of the BZDs have similar pharmacological actions; however they lack in specificity and associated with the problem of tolerance, rebound insomnia and anxiety disorders which have necessitated the search for alternatives.

Zopiclone is a newer Hypnosedative chemically unrelated to benzodiazepines; binds with high affinity to benzodiazepine receptors at the site close to rather than identical to the site occupied by BZDs. Results of the earlier studies are most contradictory since, some studies reported that Zopiclone has less potential to develop tolerance, rebound insomnia and anxiety disorders on regular use than benzodiazepines and some reported even greater potential to develop these side effects than benzodiazepines.

Present study was therefore designed to investigate whether tolerance is developed to hypnosedative activity on repeated administration of Zopiclone (7.5 mg/kg) daily.

### Experimental approach

For evaluation of development of tolerance to its hypnosedative actions animals were treated with respective drug i.e. control group (0.1ml NS), standard group (Lorazepam 5mg/kg p.o.) and test group (Zopiclone 7.5mg/kg p.o.) for 10 consecutive days; and on 10<sup>th</sup> day Pentobarbitone sleeping time potentiation & Elevated plus maze performance test were performed. The observations of 10<sup>th</sup> day compared with observations on day one.

### Results

Zopiclone (7.5 mg/kg) on chronic administration did not develop tolerance to hypnotic activity; instead this activity was increased but it was statistically insignificant i.e.  $P > 0.05$ . Similar results were observed for anxiolytic activity.

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## Conclusions

Zopiclone can be recommended as substitute for conventional hypnosedative for short term (1 – 4 weeks) treatment of insomnia, or alternatively, long term infrequent treatment of insomnia.

## Keywords

Elevated plus Maze Hypnosedative Tolerance, Zopiclone

## Introduction

Effective and safe Hypnosedatives exist especially since the introduction of benzodiazepines (BZD) which appeared to bring major advantages over barbiturates. Ideally a new Hypnosedative should induce and maintain hypnosedation without producing residual effect during the day and should be devoid of tolerance and dependence potential. However rapid development of tolerance to the hypnosedative effects is the major drawback of Benzodiazepines used for treatment of insomnia and anxiety. With regular use the original dose of the drug become progressively less effective and a higher dose is required to obtain the original effect. The development of tolerance is one of the reasons people become dependent on benzodiazepines, and also sets the scene for the withdrawal syndrome.<sup>1</sup>

Zopiclone is the first compound developed which is chemically unrelated to benzodiazepines yet binds with high affinity to benzodiazepine receptors at the site close to rather than identical to the site occupied by BZDs<sup>2</sup>. In a manner similar to benzodiazepine anxiolytics, Zopiclone has anti-anxiety, anticonvulsant, sedative, muscle relaxant and antiaggressive properties in rodents<sup>3,4</sup>.

Cyclopyrrolones (Zopiclone) a newer non-benzodiazepine Hypnosedative class has been reported to induce less tolerance, rebound insomnia and dependence than benzodiazepines even after long-term exposure<sup>5-7</sup>. Thus, with its short duration of action and good tolerability profile, Zopiclone could be a good alternative to the benzodiazepine hypnotics and may be particularly beneficial in those patients unable or unwilling to tolerate the residual effects and rebound insomnia associated with many other hypnotic agents on chronic use<sup>8</sup>. However the data on these effects is most contradictory; in contrast to the studies stating low tolerance and minimal occurrence of rebound insomnia with Zopiclone, some studies reported that Zopiclone has an even greater potential to

produce tolerance and rebound insomnia and anxiety disorders than benzodiazepines and has been described as a "benzodiazepine in disguise"<sup>9,10</sup>

Present study was therefore designed to investigate whether tolerance is developed to hypnosedative activity on repeated administration of Zopiclone (7.5 mg/kg) daily. The results obtained from this study may add more information in existing data on efficacy-tolerance of Zopiclone which may be new addition to hypnosedative armamentarium.

## Materials and methods

Present study has been conducted at Government Medical College, Miraj. The experimental protocol was approved by Institutional Animal Ethics Committee (IAEC).

## Experimental animals

Albino mice of either sex weighing 20-25gms, bred in Central Animal House (CAH) facility of the Government Medical College, Miraj were used for the study. The animals were housed under standard laboratory conditions, maintained on natural light and dark cycle and had free access to food and water. They were acclimatized to laboratory conditions before the experiment. Pre-experiment screening for righting reflex was done 1 day prior to rule out CNS disorientation. The animals that show positive righting reflex were selected for study. All experiments were carried out in daylight.

## Drugs and doses

Doses were selected from earlier studies. Lorazepam (Ativan 2mg tablet obtained from Wyeth Lederle Ltd.) dissolved in DW given orally in the dose of 5mg/kg. Zopiclone (Zopicon 7.5mg tablet; obtained from Intas Pharmaceuticals Ltd.) suspended in 0.25% CMC, given orally in the dose of 7.5mg/kg and Pentobarbitone sodium dissolved in DW; given IP in the dose of 40mg/kg.

## Test methods

Animals were divided into various groups in such way that 6 animals were there in each group. Group-A received 0.1ml NS orally served as control for all experiments except righting reflex test where animals received Pentobarbitone (40mg/kg) IP as control, Group -B received Lorazepam (5mg/kg) served as standard & Group -C received Zopiclone (7.5mg/kg). Each animal was treated with respective drug 30 min before experimentation. Following are the details of experiments performed,

### 1. Righting reflex test:

Drugs like barbiturates induce hypnosis by CNS depression easily determined by loss of righting reflex. In righting reflex test animal is kept gently on its back over an undulated surface, normally it corrects immediately; if retained on back for 30secs or more it is recorded as loss of righting reflex. Loss of righting reflex is taken as index

of CNS depression<sup>11</sup>.

### 2. Pentobarbitone sleeping time potentiation:

Pentobarbitone (barbiturate) produces quick onset of sleep as indicated by loss of righting reflex and recovery is also easily detected as the animal regain righting reflex. Animals in all three groups received the respective drugs and 30 min later treated with Pentobarbitone (40mg/kg) IP. The time interval between loss of righting reflex and reappearance of righting reflex is recorded as duration of sleep. The animal that corrects itself 3 times in 1 min is considered to have recovered from drug effect<sup>12</sup>.

### 3. Elevated plus maze performance:

The apparatus consisted of two open arms (16 cm x 5 cm) and two closed arms (16 cm x 5 cm x 12 cm). The closed arms were painted black. The arms extended from a central platform (5 cm x 5 cm), and maze was elevated to a height of 25 cm from the floor. The open arms edges were 0.5 cm in height to keep the mice from falling and the closed-arms edges were 12 cm in height. The drugs and treatments were same as mentioned under test methods. The animal was placed at the center of the maze, facing one of the closed arms. During 5 min test period the following parameters were recorded, 1. The number of entries into open arms 2. Time spent in the open arms 3. Number of animal giving preference to open arm as first arm entry. Arm entry was counted when the animal had placed all of its four paws on it. The procedure was conducted in a sound attenuated room<sup>13-16</sup>.

### 4. Test to evaluate development of tolerance to hypnotic action:

The animals were treated with respective drugs for 10 consecutive days. On 10<sup>th</sup> day of experiment 30 min later the respective drug administration pentobarbitone sleeping time was determined in all groups as described earlier. Decrease in pentobarbitone sleeping time was taken as criteria for development of tolerance to hypnotic action<sup>17</sup>.

### 5. Test to evaluate development of tolerance to Anxiolytic action:

The animals were treated with respective drugs for 10 consecutive days. On 10<sup>th</sup> day of experiment 30 min later the respective drug administration Elevated plus maze performance test was carried out in all groups as described earlier. During 5 min test period the total time spent by each animal in the open arms was recorded. Decrease in time spent by each animal in the open arms was taken as criteria for development of tolerance to anxiolytic action<sup>18</sup>.

### Statistical analysis:

Data analyzed by Student's unpaired' test and Chi-square( $X^2$ ) test. All the results were expressed as mean ( $\pm$ SEM).  $P < 0.05$  was considered significant.

## Results

### 1. Righting reflex test:

Zopiclone did not inhibit righting reflex at dose of 7.5 mg/kg like Pentobarbitone (Table 1).

### 2. Pentobarbitone sleeping time potentiation:

In the potentiation of Pentobarbitone sleep test, Zopiclone significantly increased the sleeping time in mice at dose of 7.5 mg/kg compared to controls ( $P < 0.001$ ) and Lorazepam 5mg/kg ( $P < 0.05$ ) indicating potent hypnotic activity (Table 1).

### 3. Elevated plus maze performance:

Zopiclone (7.5 mg/kg) showed significant Anxiolytic activity in Elevated plus maze performance test compared to Lorazepam as indicated by increased number of entries into open arms, time spent in the open arms and number of animal giving preference to open arm as first arm entry (Table 2)

### 4. Tests to evaluate development of tolerance to hypnotic and anxiolytic actions:

Zopiclone (7.5 mg/kg) on chronic administration did not develop tolerance to hypnotic activity; instead this activity was increased but it was statistically insignificant i.e.  $P > 0.05$ . (Table 1) Similar results were noted for anxiolytic activity (Table-2).

## Discussion

### Righting reflex test and Pentobarbitone sleeping time potentiation:

Barbiturate like drugs produce hypnosis by CNS depression determined by absence of righting reflex; however hypnosis produced by BZDs did not inhibit righting reflex suggestive of more selective actions and lack of neuronal depression. Present study clearly demonstrated that Zopiclone (7.5mg/kg) didn't cause neuronal depression. Furthermore it showed potent hypnotic activity determined by significant potentiation of Pentobarbitone sleeping time compared to Lorazepam. This potent hypnosedative activity is thought to be due to its potent agonistic activity at omega-1 receptor subtype of central BZD-receptor<sup>18</sup>.

### Elevated plus maze performance:

Animal dislike the open arm and high spaces hence spent more time in closed arm this natural aversion quality become apparent when it enters them. This is the basis for its use in the measurement of anxiety<sup>13</sup>. Present study Zopiclone (7.5 mg/kg) showed significant Anxiolytic activity in Elevated plus maze performance test compared to Lorazepam as indicated by increased number of entries into open arms, time spent in the open arms and number of animal giving preference to open arm as first arm entry.

### Test to evaluate development of tolerance to hypnotic and anxiolytic actions:

Drug tolerance is commonly encountered when a subject's reaction to a drug decreases so that larger doses are

**Table 1:** Observations in Righting reflex test & Pentobarbitone sleeping time potentiation test:

Groups (n=6)	Treatment	Righting reflex	Treatment	Duration of sleep (min) on 1 <sup>st</sup> day (Mean $\pm$ SEM)	Duration of sleep (min) on 10 <sup>th</sup> day (Mean $\pm$ SEM)
A	Control (Pentobarbitone 40mg/kg)	Absent	Control NS (0.1ml)	63.3 $\pm$ 1.2	62.3 $\pm$ 0.8
B	Lorazepam (5 mg/Kg)	Present	Lorazepam (5 mg/Kg)	85.8 $\pm$ 2.2*	82.2 $\pm$ 0.8 <sup>§</sup>
C	Zopiclone (7.5 mg/Kg)	Present	Zopiclone 7.5 mg/Kg)	<sup>a</sup> 98.5 $\pm$ 4.8*	106.3 $\pm$ 2.9 <sup>§</sup>

Each group consists of 6 animals. Values are Mean  $\pm$  SEM, data analyzed by student's unpaired 't' test. (\* $P < 0.001$  compared to control; <sup>a</sup>  $P < 0.05$  compared to Lorazepam; <sup>§</sup>  $P > 0.05$  compared to sleeping time on day one)

**Table 2:** Observations in Elevated plus maze performance:

Treatment Groups (n=6)	Dose mg/Kg	Elevated plus maze performance			
		1 <sup>st</sup> Day		10 <sup>th</sup> Day	
		<sup>a</sup> Number of animals giving preference to open arm	<sup>b</sup> Number of entries open arm to Mean $\pm$ SEM	<sup>b</sup> Total time spent open arm in Mean $\pm$ SEM	<sup>b</sup> Total time spent in open arm on 10 <sup>th</sup> day Mean $\pm$ SEM
Control (A)	NS(0.1ml)	1	4.5 $\pm$ 0.43	2.7 $\pm$ 0.25	2.6 $\pm$ 0.25
Lorazepam(B)	5	4**	6 $\pm$ 0.58	3.7 $\pm$ 0.25**	3.5 $\pm$ 0.3 <sup>§</sup>
Zopiclone (C)	7.5	5****	6.8 $\pm$ 0.48****	3.8 $\pm$ 0.31**	4.3 $\pm$ 0.2 <sup>§</sup>

Each group consists of 6 animals. Values are Mean  $\pm$  SEM, data analyzed by Chi-square( $X^2$ )<sup>a</sup> and student's unpaired 't' test<sup>b</sup>. (\* $P < 0.05$ , \*\* $P < 0.02$ , \*\*\* $P < 0.01$ , \*\*\*\* $P < 0.005$ , compared to control & <sup>§</sup> $P > 0.05$  compared to total time spent on day one)

required to achieve the same effect. Drug tolerance can involve both psychological drug tolerance and physiological factors. Characteristics of drug tolerance are it is reversible, the rate depends on the particular drug, dosage and frequency of use, differential development occurs for different effects of the same drug. There are two major mechanisms for tolerance:

- Dispositional tolerance: occurs because of a decreased quantity of the substance reaching the site it affects.
- Reduced responsiveness: the response to the substance is decreased by cellular mechanisms i.e. neuroadaptation due to chronic administration of drug.

Studies with protein-modifying agents (e.g. diethylpyrocarbonate) and photoaffinity labeling suggest that cyclopyrrolones bind to a domain on the GABA<sub>A</sub> receptor different from the benzodiazepine binding domain. The consequence of this interaction with the GABA<sub>A</sub> receptor is to potentiate responses to GABA, as can be demonstrated by electrophysiological methods.

Regular use of benzodiazepines cause down- regulation of GABA receptors hence higher dose is required to obtain desired effect i.e. tolerance is developed. However lack of tolerance to hypnosedative actions of Zopiclone observed after repeated administration is suggestive of some additional mechanism involved in its hypnosedative action i.e. apart from its GABA facilitatory action it might have effect on GABA transaminase which lowers GABA metabolism hence improves the GABA sensitivity which is not observed with benzodiazepines. Subchronic (less than 1-4 wks) treatment of mice with high doses of Zopiclone does not produce the changes in sensitivity of the GABA<sub>A</sub> receptor that is observed with hypnotic benzodiazepines<sup>19</sup>.

Our study clearly demonstrated that repeated daily administration of 7.5 mg/kg oral dose of Zopiclone for 10 days did not develop tolerance to its hypnosedative activity and these finding are in agreement with the earlier studies<sup>20-22</sup>. However extensive long-term studies for evaluating its tolerance are required for confirmation of its long-term efficacy. Zopiclone can be recommended as substitute for conventional hypnosedative for short term (1 – 4 weeks) treatment of insomnia, or alternatively, long term infrequent treatment of insomnia.

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## References

1. Ashton, H. Toxicity and adverse consequences of benzodiazepine use. *Psychiatric Annals* (1995) 25,158-165.
2. Blanchard JC, Boireau A, Garret C, Julou L In vitro and in vivo inhibition by zopiclone of benzodiazepine binding to rodent brain receptors. *Life Sci.*1979. 24: 2417-2420.
3. Sanger DJ, Joly D, Zivkovic B. Behavioral effects of nonbenzodiazepine anxiolytic drugs: A comparison of CGS 9896 and zopiclone with chlordiazepoxide. *J Pharmacol Exp Ther* 1985; 232: 831-837.
4. Julou L, Bardone MC, Blanchard JC, Garret C, Stutzmann JM. Pharmacological studies on zopiclone. *Pharmacology (Basel)* 1983. 27 (S2): 46-58.
5. Sanger DJ. The pharmacology and mechanisms of action of new generation, non-benzodiazepine hypnotic agents. *CNS Drugs*. 2004;18 Suppl 1:9-15; discussion 41, 43-5.
6. Melton ST, Wood JM, Kirkwood CK. Eszopiclone for insomnia. *Ann Pharmacother*. 2005 Oct;39(10):1659-66. Epub 2005 Aug 30.
7. Najib J. Eszopiclone, a nonbenzodiazepine sedative-hypnotic agent for the treatment of transient and chronic insomnia. *Clin Ther*. 2006 Apr;28(4):491-516.
8. Wadworth AN, McTavish D. Zopiclone. A review of its pharmacological properties and therapeutic efficacy as a hypnotic. *Drugs Aging*. 1993 Sep-Oct;3(5):441-59.
9. Bramness JG; Olsen H. "[Adverse effects of zopiclone]". *Tidsskrift for den Norske laegeforening*. 1998. 118 (13): 2029–32. PMID 9656789.
10. Luty S, Sellman D. "Imovane—a benzodiazepine in disguise". *N. Z. Med. J.* July 1993. 106 (959): 293. PMID 8321452.
11. Dandiya PC, Cullumbine H, Sellers EA. Studies on *Acorus calamus*. IV. Investigations on mechanism of action in mice. *J Pharmacol Exp Ther*. 1959 Aug; 126:334–337.
12. Dandiya, P.C. and Cullumbine, H. Studies on *Acorus calamus* (III): some pharmacological properties of the volatile oil *J.Pharmacol. Expt. Therap.*125:353-359, 1959
13. Pellow S, File SE. Anxiolytic and anxiogenic drug effects on exploratory activity in an elevated plus-maze: a novel test of anxiety in the rat, *Pharmacol Biochem Behav* 1986; 24: 525-529.
14. Itoh, J, Nabeshima, T. and Kameyama, T.: Utility of an elevated plus maze for the evaluation of nootropics, scopolamine and electro convulsive shock. *Psychopharmacology* 1990., 101: 27-33.
15. Lister, R. G. The amnesic action of benzodiazepines in man. *Neurosci Biobehav Rev*. 1985., 9: 87-94.
16. Pellow, S., Chopin, P., File, S. E. and Briley, M. Validation of open: closed arm entries in an elevated plus-maze as a measure of anxiety in the rat. *Journal of Neuroscience Methods* 1985., 14: 149–167)
17. G Perrault, E Morel, DJ Sanger and B Zivkovic Lack of tolerance and physical dependence upon repeated treatment with the novel hypnotic zolpidem. *J Pharmacol Exp Ther* October 1992 263:298-303
18. Ozawa M., Nakada Y., Sugimachi K., Akai T., Yamaguchi M. Interaction of the hypnotic lormetazepam with

- central benzodiazepine receptor subtypes omega 1, omega 2 and omega 3. *Nippon. Yakuri.Zasshi.*, 1991,98:399-408
19. A Döblea, T Cantona, C Malgourisa, JM Stutzmanna, O Piota, MC Bardonea, C Paucheta and JC Blancharda *European Psychiatry* Volume 10, Supplement 3, 1995, Pages 117s-128s Satellite Symposium to the AEP Congress
  20. Anderson, Aa. "Zopiclone and nitrazepam: a multicenter placebo controlled comparative study of efficacy and tolerance in insomniac patients in general practice." *Sleep* (1987)10 Suppl 1: 54-62.
  21. Begg, Ej; Robson, Ra; Frampton, Cm; Campbell, Je. "A comparison of efficacy and tolerance of the short acting sedatives midazolam and zopiclone." *The New Zealand medical journal* (Oct 1992);105 (944): 428-9.
  22. Dorian, P; Sellers, Em; Kaplan, H; Hamilton, C. "Evaluation of zopiclone physical dependence liability in normal volunteers." *Pharmacology.* (1983) 27 Suppl 2: 228-34.

# Comparative study of PAP smear with lower abdominal pain and per vaginal discharge: A survey in rural western UP

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## Introduction

Cervical cancer is the most common cause of death in middle aged Indian women. Pap smear, as a tool for cervical cancer screening, has gained popularity in the public health programme in cancer prevention. Cervical cancer rates have gone down by 60-90% in countries where it has been successfully implemented. Unfortunately there is very little population based cervical screening data available in our country. It is not being used routinely as an important investigation tool, as a result, nearly 1,20,000 women are detected as cervical cancer every year in India and 70-90% of them are at advanced stage of disease.

## Material and method

This is a progressive consecutive study conducted in the department of Obstetrics and Gynaecology at Saraswati Institute of Medical Sciences, Hapur, Ghaziabad, India. This study was initiated only after taking permission from institutional ethical committee. This prospective study was conducted with the aim to know the prevalence of early and late dysplastic changes and any other vaginal infections in rural areas, low socioeconomic group patients with relation to age and parity. This study was done from Jan 09-Dec 09 and all the patients coming in the gynaecological OPD with complaints of white discharge per vaginal and pain in lower abdomen were included in this study. These patients were initially examined by vaginal speculum under aseptic precaution and findings with congested, oedematous, and hypertrophic or erosion in the cervix were subjected for pap smear examination. Patients with fungating growth on cervix, menstruating ladies were excluded from this study.

With patient in supine position, a Cusco's Speculum is introduced into the vagina. After that a wooden Ayre's spatula was inserted into the external os so that its long end is placed in the external os as deeply as possible and rotated for 360 degrees, and scraping of the entire surface of external os and the part of the internal os was taken and spreaded over one slide. With the help of endocervical brush, smear from the cervical canal were also taken out and spreaded on another slide. The material thus

collected in two slides was fixed by cyto spray and sent for examination pathology department for evaluation.

Pap smear test, the only screening test for cervical carcinoma, can detect any abnormal change to the cells of the cervix as well as detect early stage of cervical carcinoma. In this test, if no abnormal cells were seen, it is labeled as negative and requires no treatment, whereas presence of abnormal cells is reported as positive. The cell abnormalities are reported as follows according to their categories:

(a) Atypical Squamous Cells (ASC): Squamous cells of cervix had turned into atypical squamous cells. According to Bethesda system, these atypical squamous cells are classified into:

(i) Atypical Squamous Cells Undetermined Significance (ASC-US)- where cells are mildly atypical.

(ii) Atypical Squamous Cells High grade (ASC-H)- where cells are moderately atypical.

(b) Low Grade Squamous Intraepithelial Lesion (LSIL): refers to early changes in the shape and sizes of squamous cells on the surface of cervix. The abnormal growth of cells refers to dysplasia.

(c) High Grade Squamous Intra epithelial Lesion: refers to moderately abnormal changes in the size and shape of the abnormal cells on the surface of the cervix.

## Observations

360 patients were included in our study who met the inclusion criteria. These patients were aged from 20 years to 64 years, with the predominance of 20 to 30 years age group. (Table-1)

Most of the patients in our study were in between para 3 and para 4 with Hindu predominance. (Table-2)

In our study 55.56% patients were suffering from pain lower abdomen while 44.44% patients had complained of white discharge per vagina. On per vaginal examination, 60% had cervicitis while 40% had cervical erosion.

On pap smear examination, out of total 216 patients, 18.51% patients had LSIL in cervicitis group while in 6.94% patients were positive in erosion of cervix. HSIL was present in 0.94% in cases cervicitis and 0.69% in cases of cervical erosion.

**Table 1:** Showing Age distribution

Age group	20-30 years	30-40years	40-50years	50-60years	>60years
No. of Pts.	156	149	44	10	1
Percentages	43.33%	41.39%	12.22%	2.78%	0.28%



Table 2: Showing Parity

Parity	Para 1to para2	Para 3 to para4	Para 5 to para6
No. of Patients.	60	250	50
Percentages	16.67%	69.44%	13.89%

## Discussions

Cervical cancer is the commonest malignancy of genital tract in Indian women. A quarter of the global burden is experienced in India <sup>1,2</sup>accounting for 20 - 50 % of all the cancers and 80-85% of all the female genital tract cancers <sup>2,4</sup>.The prognosis can be improved, if the cervical changes are identified at an early stage. Cervical cancer is preceded by a long pre-invasive phase, i.e. dysplasia or cervical intraepithelial neoplasia (CIN ). Due to slow rate of progression, if these pre invasive lesions are detected and treated with various available modalities, they virtually have a 100% cure rate. However if detected in advanced stage, the 5 year survival rate is less than 40%<sup>3,4</sup>. The identification of relevant risk factors and the detection and management of precancerous and rarely, invasive lesions of the uterine cervix are important in the prevention of invasive cervical cancer<sup>5</sup>.

In this study, females with complaints of either white discharge per vaginal or pain in lower abdomen, were taken into consideration. These patients were examined by vaginal speculum (Cuscus) and findings with cervical erosion or cervicitis were subjected to Pap smear examination. Patients with positive Pap smear reports (LSIL, HSIL) with clinically suspected cervix were subjected to cervical biopsy.

It has been found that mean parity in mild, moderate and severe dysplasia cases were 3.3, 3.5 and 3.9 respectively<sup>8</sup>. It is also reported that multiparity acts as an independent

risk factor. Studies on Indian subjects reported an increased risk of cervical cancer and HPV infection with increasing number of pregnancies <sup>7</sup>.

In this study, though a higher proportion of positivity (2.69 %) was seen among the lower socioeconomic class. Elliot had documented that cervical cancer is commoner in low socioeconomic class in whom the component of poverty, overcrowding, inadequate food and clothing, housing, hypothermia and poor personal hygiene are contributory factors to infection and malignancy. <sup>14</sup> Shah and Parkin<sup>6</sup> agreed to this view, saying that the development of cancer cervix varies with lifestyle of individual, social customs and geographical distribution. It is stated that the risk of cervical cancer is highest among blacks, poor and uneducated populations. It has been established that low-grade dysplasia are usually asymptomatic. The common complaints in high-grade dysplasia are discharge per vagina, irregular bleeding, intermenstrual and post coital bleeding per vagina<sup>10,15</sup>. Shankarnarayana et al had found that cervicitis was most common finding. He stated that visual inspection of cervix is an art, neglected in recent years in reference to cytological screening, which will reveal characteristic signs of early dysplasia<sup>4</sup>

In present study, naked eye examination of cervix revealed that the most common finding was cervicitis, seen in 216, (60%), and cervical erosion was seen in 144 (40 %) cases (Table 3). In our study 53 out of 360 pap's smears were found to be abnormal. In cases of cervicitis, LSIL was seen in 40 (18.5 %) and HSIL in 2(0.94 %) cases. In cases of cervical erosion, LSIL was present in 10 (6.94 %) and HSIL in 1(0.69 %) cases.

In our study 48.15% smears were reported as inflammatory in cases of cervicitis and 69.44% in cases of cervical erosion. In a study from India by Luthra (8) et al, 70% smears were inflammatory. Large number of cases in India has

Table 3: Showing symptoms and signs

Symptoms (n=360)		per speculum exam.(n=360)	
White discharge	pain lower abdomen	cervicitis	erosion
160	200	216	144
44.44%	55.56%	60%	40%

Table 4: Showing pap smear result

Findings	Cervicitis (n=216)		erosion(n=144)	
	No. of Pt.	Percentage	No. of Pt.	Percentage
Inflammation	104	48.15%	100	69.44%
Bacterial Vaginosis	50	23.15%	20	13.89%
Trichomonal Vaginitis	15	6.94%	9	6.26%
AUCUS	5	2.31%	4	2.78%
LSIL	40	18.51%	10	6.94%
HSIL	2	0.94%	1	0.69%

Table 5: Showing age wise distribution of lsil & hsil

Age Group	20-30 YEARS	30-40 YEARS	40-50YEARS	50-60YEARS
LSIL(n=50)	13(26%)	23(46%)	9(18%)	5(10%)
HSIL(n=03)	0	0	2(66-67%)	1(33.33%)

### The result of our study was comparable to the study of Luthra et al and Cuzick et al.

Pap Report	Luthra (8)	Cuzick(9)	Cronje(10)	Present study Cervicitis/ Erosion
Mild dysplasia	0.87%	1.7%	LSIL 3.6%	18.51%/ 6.94%
Moderate dysplasia	0.4%	1.1%	HSIL 4.7%	0.94%/0.69%
Severe dysplasia	0.07%	0.9%		
CIS			1.0%	
Malignancy	0.9%			

inflammatory report on cytology. This is probably one of the risk factors for the development of cervical cancer in Indian scenario.

Cervical biopsy was done in 20 patients who either have positive pap's smear report or suspicious cervix. 17 patients were found to be having Mild dysplasia and 3 patients had moderate or severe dysplasia.

Pap's smear as a screening test has been shown to have a sensitivity ranging from 51-84%<sup>11,13</sup>. False negative smears were high ranging from 25-48%.

### Conclusion

We are concluding our study that pap smear should be recommended in all patients who are complaining either pain in the lower abdomen or per vaginal discharge to prevent the chances of early cervical dysplastic changes and to diagnose the carcinoma cervix in its early stage. It is evident that this small investigation, if performed routinely in these patients, better prognosis can be expected. This can reduce the occurrence of invasive carcinoma of cervix in India.

### References

- Parkin DM, Bray F, Ferlay J et al. Estimating the world cancer burden: Globocan 2000;. *Int J Cancer* 2001;94:153-6.
- Shankarnarayana R, Nene BM, Dinshaw K, Rajkumar R, Shasstri S, Wesley R, et al. Early detection of cervical cancer with visual inspection method: a summary of completed and ongoing studies in India. *Salud Publica de Mexico* 2003;45(12):274-82 .
- Dinshaw KA, Rao DN, Ganesh B. Tata Memorial Hospital Cancer Registry annual reports Mumbai, India. 1999; 52.
- Shankarnarayanan R, Black RB, Parkin DM, eds. *Cancer Survival in developing countries*. Lyon: IARC Press. 1998; ( IARC Scientific Publication No. 145 )
- Richart RM, Barron BA. A follow up study of patients with cervical dysplasia. *Am J Obstet Gynecol* 1969; 105:386.
- Shah M., Parkin B. Epidemiological study of the cancer of the uterine cervix in adivasi people of five different states of India. *J Obst Gynae of India* 1985;335:335-60..
- Gopalkrishna V, Murthy NS, Sharma JK, Roy M et al. Increased Human papilloma Infection with increasing number of pregnancies in Indian Women. *J Infect Dis* 1995; 171: 254-55.
- Luthra UK, Prabhakar AK, Seth P, Agarwal SS, Murthy NS, Bhatnagar P, Das DK, Sharma BK. Natural history of precancerous and early cancerous lesions of the uterine cervix. *Acta Cytol* 1987; 31 (3 ): 226-34.
- Cuzick J, Szarowski A, Terry G, Ho L Hanby A, Maddox P, Anderson M, Kocjan G, Steele ST, Guillebaud J. Human Papilloma virus testing in primary cervical neoplasia in a developing country. *Am J Obstet Gynecol* 2003; 188:395-400.
- Cronje HS, Parham GP, Cooreman BF, de Beer A, Divall P, Bam Rh. A comparison of four screening methods for cervical neoplasia in a developing country. *Am J Obstet Gynecol* 2003; 188:395-400.
- Soost HJ, Lehmacher W, Ruffinger, Kullman B. The validation of cervical cytology- sensitivity, specificity and predictive value. *Acta Cytol* 1991; 35 (1): 8-14.
- Vander Graff, Voojjs GP: False negative rates in cervical cytology. *J Clin Pathol* 1987; 40: 438-442.
- Gay JD , Donald LD, Goellner JR. False negative results in cervical cytological studies. *Acta Cytol* 1985; 29: 1043.
- Elliot RIK. On prevention of carcinoma of cervix. *Lancet*. 1964; 1: 232.
- AC. Anonymous: Black-White difference in cervical cancer mortality, United States, 1980-1987. *MMWR*1990; 39:245.

# Comparison and correlation of glucose levels in serum and saliva of patients with diabetes mellitus

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## Abstract

### Background and objectives

In Diabetes Mellitus, an important aspect of glycaemic control is to regularly monitor glucose levels. Current methods employed, either require a blood sample or urine sample. These procedures usually cause pain and discomfort to the patient. Hence, arises the need for a non-invasive technique in diagnosis and in monitoring glycaemic status of an individual. The study was undertaken in an attempt to compare and correlate glucose levels in saliva and serum of patients with diabetes and non-diabetic healthy individuals, to determine the efficacy of saliva as a diagnostic aid.

### Method

250 individuals visiting diabetic clinics were screened randomly. Of these, 200 were confirmed diabetics and were under medication (Study Group). The remaining 50 gave neither a past history of diabetes nor did their present glycaemic status depicted high values (Control Group). Venous blood and salivary samples were obtained from each individual and subjected to glucose estimation. Both fasting and post-prandial samples were analyzed.

### Results and observations

Glucose was detected in the saliva of both diabetic and non-diabetics. The fasting salivary glucose values in the control group ranged from 4.1 to 13.3 mg/dl and the post-prandial salivary glucose values from 12.5 to 20.0 mg/dl. The fasting salivary glucose values in the study group ranged from 4.1 to 26.6 mg/dl and the Post-prandial salivary glucose values from 15.3 to 30.7 mg/dl. It was observed that as blood glucose levels changed in both fasting and post-prandial samples, so did salivary glucose levels, irrespective of age and sex.

A significant P value < 0.001 and positive correlation was found between blood glucose and salivary glucose levels in both the diabetics and the controls.

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## Conclusion

It can thus be inferred that saliva can be used as an adjunct diagnostic tool in Diabetes Mellitus.

## Keywords

Diabetes Mellitus, glycaemic status, salivary glucose, non invasive diagnostic tools in Diabetes, saliva in diabetics.

## Introduction

Diabetes mellitus (DM) is a complex multi-system disorder characterized by a relative or absolute insufficiency of insulin secretion and / or concomitant resistance to the metabolic action of insulin on target tissues.<sup>1</sup> There is a need to implement preventive measures to reduce the high morbidity and mortality and also to reduce the cost burden to the patients and to the society.<sup>2</sup>

An important aspect in glycaemic control is to regularly monitor blood glucose levels. Current methods employed in monitoring require either a blood or a urine sample. Obtaining blood samples is painful and difficult for diabetics who may have to repeat the procedure several times. Urine samples have also been used for analysis; however patients often face problems of discomfort. The obtained results have known to depict many discrepancies. As a diagnostic fluid, saliva offers distinctive advantages over serum. It can be collected non-invasively with modest training and without use of any sophisticated equipment. The chances of infection are lowered and disposal of associated wastes, poses a lesser health hazard. Furthermore saliva may provide a cost effective approach for screening large populations. Diagnosis, via the analysis of saliva is potentially valuable, as the collection of this fluid is associated with fewer compliance problems as compared to the collection of blood or urine.<sup>3</sup> Thus, the study was undertaken in an attempt to compare and correlate glucose levels in saliva and serum of patients with DM and non-diabetic healthy individuals, to determine the efficacy of saliva as a diagnostic aid.

## Materials & method

In this study, of 250 patients, 200 were known cases of type II diabetes mellitus and were on medication. They were included in the study group. The remaining 50 patients had neither a previous history of diabetes nor did their current glycaemic status reveal high glucose levels. They were included in the control group. Presence of an obvious oral

lesion, patients treated for any salivary gland disorders, patients on medication for any other local or systemic diseases other than diabetes mellitus were excluded from the study. A detailed case history regarding duration of disease, family history and associated habits were noted. The patients were briefed on the study and a written consent was obtained following which, an intra-oral examination was done and the findings were recorded. Patients with apparently normal oral mucosa were included in the study. The patients were then advised to come back for collection of fasting and post-prandial samples of both saliva and serum on the following day. The study was reviewed and approved by the ethical board of the institute.

Unstimulated whole saliva was collected via the 'spitting method'. It was ensured that all the patients rinsed their mouth thoroughly prior to sample collection. This was done to eliminate the chances of food residue providing a source of glucose. Also the samples collected were immediately subjected to analysis, to avoid deterioration of the sample due to incubation and also, to avoid enzymatic alteration of glucose in saliva.

### Detailed procedure

1ml of saliva was taken into a disposable test tube and centrifuged at 2000 rpm for 2-3 min. Using a micro-pipette, 1 ml of the glucose reagent was taken in another test tube. Next, 10µl of the supernatant of the centrifuged saliva sample was obtained and added to the glucose reagent. This was then kept in a temperature controlled water bath at 37°C for 10 minutes. The color change was noted and the optical density (OD) was measured in a photo-colorimeter (BIOZYME LIQUID GLUCOSE KIT, BIOMEDIX) based on the principle of enzymatic colorimetry. Under aseptic conditions 2 ml of the patient's intra-venous blood was obtained from the median cephalic vein of the forearm, using a 25 gauge, 5 ml disposable syringe. Serum was obtained and subjected to the same procedure as that of saliva. The fasting glucose levels and post prandial glucose levels in both saliva and serum were calculated for the study group and control group. Statistical analysis was done using unpaired Student's t test.

### Results

Of the 200 diabetic cases 108(54%) were males and 92(46%) were female patients. Of the 50 controls, 28(56%) were males and 22(44%) were female subjects. The mean age of the diabetic patients was 51.65±10.22. The mean age of the control group was 46.68±9.59.

The current diabetic status of the study group of 200 patients was estimated, among which 65 individuals had a fasting blood sugar (FBS) below 126 mg/dl and were well within the range of glycaemic control. The remaining 135 patients had a FBS > 126 mg/dl.

FBS values in the control subjects ranged from 75 to 120 mg/dl with an average of 95.58 ± 12.01. The Fasting salivary sugar (FSS) values ranged from 4.1 to 13.3 mg/dl with a mean of 9.20 ± 3.33 mg/dl. Post-prandial blood sugar (PBS) values in control subjects ranged from 100 to 140 mg/dl with an average of 117.5 ± 13.143 mg/dl. The Post-prandial salivary sugar (PSS) values ranged from 12.5 to 20.0 mg/dl, with an average of 14.65 ± 2.26 mg/dl (Table 1).

In the study group, 86 patients had a FBS ranging between 80 to 140 mg/dl and a corresponding FSS value of 4.1 ± 19.2 mg / dl. An additional 31 patients had similar FSS levels but correspondingly higher FBS levels. 24 patients had a FBS of 181 to 200 mg / dl and an FSS of 23.1 ± 26.6 mg / dl while 21 other patients had a similar blood glucose level but correspondingly lower salivary glucose levels. For the post-prandial values recorded, 144 patients had a PBS of 140 to 200 mg/dl and a PSS of 15.3 to 23.3 mg / dl. An additional 11 patients recorded similar PSS levels but higher PBS levels. In the higher range of 200 to 280 mg / dl PBS and 23.4 to 30.7 mg/dl PSS, 45 patients were enlisted. An additional 11 patients showed similar blood glucose levels but correspondingly lower salivary glucose levels (Table 2).

It was inferred from this study that the salivary glucose levels correspondingly increase / decrease as the blood glucose levels increase / decrease respectively. The FBS and FSS values and the PBS and PSS values were found to be correlated positively and significantly (p<0.001).

The high sensitivity of 99.25% achieved in this study is indicative of the fact that saliva can serve as a good screening tool in diagnosis of DM. From the specificity of

**Table 1:** Glucose levels in control group

FBS inmg/dl (No. of Patients)	FSS inmg/dl (No. of Patients)	PBS inmg/dl (No. of Patients)	PSS inmg/dl (No. of Patients)
75-85(20)	4.1 - 6.6(20)	100 - 120(35)	12.5 - 16.0(40)
86 - 95(14)	11.5 - 12.0(13)	121 - 130(7)	16.1 - 16.6(5)
96 - 120(16)	12.1 - 13.3(17)	131 - 140(8)	16.7 - 20.0(5)

**Table 2:** Glucose levels in study group

FBSmg/dl(No. of Patients)	FSSmg/dl(No. of Patients)	PBSmg/dl(No. of Patients)	PSSmg/dl(No. of Patients)
80 - 140(86)	4.1 - 19.2(117)	140 - 200(144)	15.3 - 23.3(155)
141 - 180(69)	19.3 - 23.0(59)	201 - 240(37)	23.4 - 26.6(30)
181 - 200(45)	23.1 - 26.6(24)	241 - 280(19)	26.7 - 30.7(15)

61.73% that was obtained in this study, it can be inferred that although saliva can serve as an adjunct diagnosis tool, it fails to be labeled as a definitive diagnostic tool. Hence although saliva can aid in diagnosis of DM, a confirmatory blood glucose analysis is mandatory. The predictive value of a positive test in this study was 75.28% indicating the probability of the number of patients who showed high glucose levels in saliva also showed high glucose levels in blood. The predictive value of a negative test in this study was 98.6% indicating the probability of the number of patients who did not show elevated salivary glucose levels as well as blood glucose levels.

## Discussion

Diabetes mellitus is a complex group of syndromes that have in common a disturbance in the body's use of glucose, resulting in elevated blood glucose. Blood glucose monitoring by the patient and the physician is an important aspect in the control of the devastating complications due to the disease. With ever improving advances in diagnostic pathology, the race for the next generation of bloodless, painless and accurate glucose instruments has begun. Most commonly used laboratory diagnostic procedures involve the analysis of blood, but other biological fluids are also being utilized for the diagnosis of other diseases and of these, saliva offers distinctive advantages.<sup>4</sup> Biochemical analysis of saliva in diabetic patients revealed the increased presence of calcium and certain organic constituents like protein, glucose, amylase, lysozymes, lactoferrin, urea and immunoglobulins.<sup>5</sup> The increased presence of certain inorganic and organic constituents in saliva of diabetic individuals could be attributed to the increased basement membrane permeability of exocrine glands, often seen in diabetes.<sup>6</sup>

The possible effects of raised serum glucose of diabetic patients on the level of glucose in saliva and other tissue fluids has long been the subject of research and controversy.<sup>5,7</sup>

Studies have shown smokers to have a poorer glucose control than non smokers as the body is less able to respond to insulin.<sup>8</sup> However in the present study no correlation was found between smokers and their glucose levels in either blood or saliva.<sup>11</sup>

Diabetes is known to be associated with an increased risk of periodontal diseases. The severity of periodontitis is proportional to the glycaemic level of the patient. Apart

from the role of micro organisms, the increased risk of periodontitis in DM may be influenced by hyperglycemia associated reduction in cell proliferation and growth and the synthesis of collagen and glucosaminoglycans.<sup>1,9,10</sup> In the present study, glucose values obtained for fasting salivary and post prandial salivary samples were found to be higher in diabetics than controls. It was observed that as FBS levels change so does FSS and as PBS levels change so does PSS, thus depicting a strong correlation between blood glucose and salivary glucose.

## Conclusion

Thus from the present study, it is inferred that salivary glucose levels can be detected in both diabetic and healthy individuals. In conclusion, saliva can serve as an adjunct diagnostic aid in DM

## References

1. M Manfredi, M J Mc Cullough, P Vescovi, Z M Al Kaarawi, S R Porter. Update on diabetes mellitus and related oral diseases. *Oral Diseases* 2004;10:187-200.
2. A Ramachandran, C Snehalatha, Vijay Viswanathan. Burden of type 2 diabetes & its complications – The Indian scenario. *Current science* 2002;83(12):1471-75.
3. Eliaz Kaufman, Ira B Lamster. The diagnostic applications of saliva – A Review. *Crit Rev Oral Biol Med* 2002;13(2):197-212.
4. Yarat A, Tunali T, Pisisiciler R, Akyuz S, Ipbuker A, Emekli N. Salivary thromboplastic activity in diabetes and healthy controls. *Clin Oral Investing* 2004;8(1):36-9
5. K K Mehrotra, T N Chawla. Quantitative estimation of salivary glucose. *J Indian Dental Assoc* 1968;40:243-8.
6. Murrah V A, Crusson J T, Sauk J J. Parotid gland basement membrane in diabetes mellitus. *J Oral Pathol* 1985;14:236-46.
7. Darwazeh AMG, MacFarlane TW, McCuish A, Lamey P J. Mixed salivary glucose levels and candidal carriage in patients with diabetes mellitus. *J Oral Pathol Med* 1991;20:280-83.
8. Ryan M E, Carnu O, Kamer A. The influence of diabetes on periodontal tissues. *JADA* 2003;134:34-40.
9. Kapur A and Jorgensen L.N. Diabcare Asia – current status in India. *Diabetes Research & Clinical Practice* 2000;50(1):137.
10. Mathews D C. The relationship between diabetes and periodontal disease. *J Can Dent Assoc* 2002;68(3):161-64.

# Transgenic animals and drug development: A review

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## Abstract

Pharmaceutical companies face the challenge that only ten percent of compounds tested in clinical trials eventually make it to the market and out of these, only a few will succeed to generate profit. Utilization of genetically altered animals (transgenic animals) in the pharmaceutical industry provides important insights into the function and interaction of particular gene products. Now, with the help of advanced technology numerous transgenic animals have been produced. The advent of transgenic animals has influenced the attrition rate in pharmaceutical research and development by increasing the quality of both targets and compounds. As with any experimental animal model, transgenic animals also have certain limitations but still they provide a powerful tool for the advancement of drugs in the pharmaceutical industry.

## Keywords

Animals; Experiment; Drug.

## Introduction

Animals with specific genetic alteration are referred to as transgenic animals. The term transgenic refers to the introduction of a foreign gene (known as transgene) into the genetic material of mouse in both the germ cells and somatic cells. This process leads to the expression and propagation of the gene across future generations.

Since the completion of the human and mouse genomes; the focus in mammalian biology has been on assessing gene function. The close similarity of gene function and physiology between mice and humans, and that approximately 99% of all human genes have a counterpart in the mouse genome with the genomic sequence of both organisms now available, the strategy may be used as a powerful tool for understanding human genes. (1)

Development of transgenic animals provides an exciting array of experimental strategies that offer new opportunities for understanding the complex nature and mechanisms of human diseases. Genetic studies in humans are costly and long term. The mouse study could be performed five times faster cost just 1% of that of human study (2). Genetic models in rats are more difficult to produce as they rely on untargeted germ line mutagenesis hence mouse is the preferred animal for transgenic models. (3)

## History

In 1974 Janenisch and Mintz first demonstrated that foreign DNA could be introduced into fertilized mouse eggs and then detected in various tissues of the transgenic mice that developed from these embryos. (4). The early publications were from the labs of Palmiter and Brinster in 1982-83 (5) (6) describing the spectacular giant mice, over expressing growth hormone. The first knockout mice were produced by Mario Capecchi, Martin Evans and Oliver Smithies in 1987-89. (7)

## Prerequisites

Generation of transgenic animals requires the knowledge of certain principles like:

- The gene regulatory mechanisms of the animal should be known.
- Well characterised transcriptional regulatory elements, promoters or enhancers, which direct transgene expression in specific cell types, should be available.
- It should be possible to produce specific molecules and also to achieve the blockage of specific biological pathway.

## Types

Based on the genetic alteration involved, transgenic animals can be of three types as below:

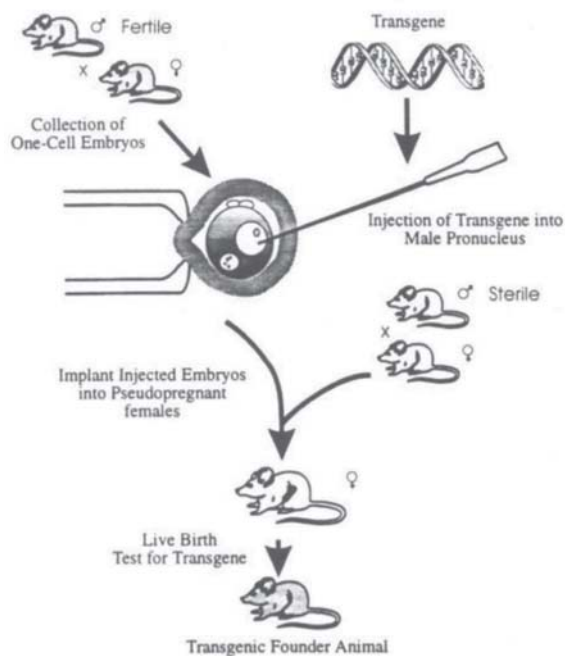
- Knock out animals- inactivation or disruption of existing gene/genes.
- Knock in animals- insertion of new gene/genes of interest.
- Knock down animals- partial suppression or expression of gene/genes.

## Methods of production

The traditional methods involved in generation of transgenic animals include:

1. Pronuclear DNA Microinjection: Here a piece of recombinant DNA with gene of interest is constructed and engineered in a specific way followed by the injection of such DNA into nuclei of fertilised embryo at one cell stage. The disadvantage with this method is that it results in an unpredictable number of transgene copies being incorporated at random locations in the recipient genome. To counter for such

effects multiple independent lines of transgenic mice need to be established for each experiment.(8)



2. Embryonic Stem Cell Transfer: The embryonic stem cells which could maintain their pluripotent characteristic in culture are isolated from certain stages of embryo, the gene of interest is manipulated followed by transfer of these altered embryonic stem cells back to embryos at appropriate developmental stages (usually the blastocyst stage) for production of chimeric mice. The advantage of this method is specific mutations can be induced by gene targeting to avoid the problems of non specific sites.
3. Conditional Mutagenesis: Here the introduced genes are engineered in a way to express in particular cell types and such that they can be switched on and off by an external signal. Thus allowing the animal to develop normally.

### Inducible expression of genes

The most rapid transgenic animal which can be produced is the one that over expresses the transgene either ubiquitously or in a tissue specific manner. The

reproducibility and the consistency of a response rely on the stable integration and heritable germline transmission of the transgene that is incorporated into the mouse genome. It is critical that the transgene remains stably integrated through the breeding of multiple generations of the transgenic mice. (9) Chronic expression of a transgene could cause a developmental abnormality or adaptation, leading to masking or distortion of the acute role of protein of interest. (10) To avoid the complication of functional or developmental compensation or drastic developmental phenotypes, temporal control over transgene expression is desirable.

To control the location or time of transgene expression, transgene promoters are used to target its expression to a specific tissue or period of organogenesis. Promoters are stretches of DNA associated with a specific gene that guide the expression of the gene "on" either before birth or after birth. Thus, promoters act as inducible elements and facilitate exogenous control of gene expression. (11)

A large number of tissue specific promoters have been used to restrict transgene expression to different cell types. Metallothionein promoter was the first to be used followed by phosphoenol pyruvate carboxykinase promoter. (12) It was difficult to regulate and control background expression with these promoters. Today the most commonly used systems for transgene regulation are:

- i. Tetracycline system (13)
- ii. cre/Lox system from bacteriophage P1 (14)
- iii. flp/frt system from yeast
- iv. modified estrogen Ligand-Binding Domain (LBD) system
- v. glucocorticoid system
- vi. interferon  $\alpha$  system

### Scope

The transgenic approach offers opportunity to create animal models with well defined systematic genetic alterations that can be used to study normal and abnormal processes involved in disease. The following are the opportunities provided by transgenic animals: (25)

- Understanding the control and regulation of gene expression
- Understanding cellular functions by targeted gene

**Table 1:** Examples of Some Popular Transgenic Animals

System	Disease	Transgenic Animal model
CNS	Alzheimer's Parkinson's- Epilepsy- Alcohol Research	APP751 over expressing mice, Presenilin 1 mice,(15) Synuclein over expressing miceDBA/2J mice, Totterer mice, Genetically Epilepsy-prone rats (GEPRs) (16) ADH1 mutant mice(17), PKC $\alpha$ mutant mice,(18)
CVS	Hypertension Atherosclerosis	Transgenic rats over expressing the Mouse Ren-2 GeneLDLr <sup>-/-</sup> and ApoE Knockout mice (19)
Endocrine	Diabetes Mellitus Obesity	db/db mouse(20), KK mouse, Zucker diabetic Fatty rat (21)ob/ob mice(22), New Zealand Obese(NZO)mouse(23)
Carcinoma		Nude mouse model,(24)

ablation

- Identification of new genes and proteins by insertional mutagenesis
- Developing new animal models of human diseases
- Developing new therapeutic approaches
- Producing new cell lines

## Applications of transgenic animals

Genetically altered mice are used in drug discovery research to characterize the diverse functions of one or multiple gene products and to establish animal models of human disease for proof of concept studies. Transgenic technology can impact at many points in the drug discovery process like:

1. Defining potential therapeutic targets for modifying physiological responses i.e., target identification and validation (increasing the quality of target compounds).
2. Providing better models for human diseases; new and appropriate disease models can be generated by transgenic technology. The closer the match, the greater the predictive value of using the disease models.
3. Humanised transgenic animals harbouring the human target molecule can be used to understand the effect of a compound acting on the human target in vivo.
4. Models resembling human drug metabolism will provide a means of assessing the effect of human-specific metabolites and of understanding the pharmacokinetic properties of potential drugs.
5. In toxicology studies, transgenic animals provide more predictive models, especially to look for carcinogenicity associated with new compounds. Using transgenic animals may reduce the total number of animals needed for such studies.
6. Gene expression analysis can be used to discover new targets and also to disclose the linkage between genes and disease.
7. The greater use of transgenic models in drug discovery process could reduce the require throughput for achieving success and thereby, significantly impact on costs.

The advantage with transgenic technology is that, the genetic alteration introduced is inherited and only needs to be generated once. Breeding can produce many such animals thus facilitating the research community. The ability to study the disease onset and progression in a highly controlled environment becomes easier.

Limitations and Issues Concerned with Transgenic Animals:

The genetic approach is tedious and labour intensive. Majority of the diseases are polygenic and hence genetic analysis becomes complicated. Since many biological response pathways are subject to polygenic control, single gene manipulations may be insufficient for understanding exposure-response relationships. (9). Likewise some other problems associated with transgenic animals are:

- i. Certain transgenic phenotypes may result in lethality

that may compromise animals' health status like impaired reproduction/lactation, immunodeficiency etc., which may preclude further evaluation of the gene product in adult knockout mice. (8).

- ii. During development there may be physiologic compensation for the loss of a gene product in the knockout mouse, thus complicating the interpretation of the phenotypic changes seen in transgenic animals.(26)
- iii. One transgenic mouse will not be identical to another. In addition, strain differences will be a source of variability.
- iv. Highly inbred nature and homogeneity in the transgenic animals is unlike heterogeneity seen in human diseases.
- v. Incorporation of new genetic material may alter the control or function of other genes.
- vi. Limited availability, expensive nature and requirement of sophisticated maintenance are some of the common disadvantages with transgenic animals. (27).

In summary, well characterised, genetically stable animals maintained in a well defined controlled environment that is free of pathogens will facilitate the evaluation of transgenic animals.

Sources of Information: Database containing information pertaining to the numerous transgenic animals have been generated. The Jackson Laboratory has a large collection of transgenic animals developed in-house by scientists and these can be requested by interested researchers. (28, 29)

### Some of the internet web sites addresses for products and services related to transgenics is given below:

Address	Website
1. Jackson Laboratory	<a href="http://www.jax.org">www.jax.org</a>
2. Mouse genome database	<a href="http://www.informatics.jax.org">www.informatics.jax.org</a>
3. Mouse and Rat Research Home Page	<a href="http://www.cco.caltech.edu">www.cco.caltech.edu</a>
4. Oak Ridge National Laboratory	<a href="http://ornl.gov">http://ornl.gov</a>
5. TBASE: Transgenic and targeted mutation database	<a href="http://tbase.jax.org">http://tbase.jax.org</a>

## Conclusion

The discovery and risk assessment of pharmaceutical compounds will continue to benefit from the advancements of transgene and gene-targeting technology. Studies in transgenic animal lines result in fewer false-negative and false-positive outcomes. Fewer indeterminate results would facilitate the risk assessment process. This would benefit pharmaceutical industries, regulatory review process and public. Transgenic technology represents an attractive approach to reducing the attrition rate of compounds entering clinical trials by increasing the quality of the target compounds making the transition from discovery into development.



## References

1. Luthra PM, Singh J, Kumar R, Singh S. Role of Geneknockout Strategy in New drug Discovery. In: Kohli K, Gupta M, Tejwani S editors. Contemporary Perspectives on Clinical Pharmacotherapeutics. Elsevier, 2006:124-144.
2. Paigen K, Eppig JT. A mouse phenome project. *Mamm. Genome*, 2000, 11: 715-717.
3. Marks CL. Animal Models for Human Diseases: Is There a Future Without Them? *The Journal of Nuclear Medicine* Dec 2006, 47(12):50N-51N.
4. Jaenisch R, Mintz B. Simian virus 40 DNA sequences in DNA of healthy adult mice derived from preimplantation blastocysts injected with viral DNA. *Proc. Natl. Acad. Sci. USA* 1974, 71:1250-1254.
5. Palmiter RD, Brinster RL, Hammer RE, et al. Dramatic growth of mice that develop from eggs microinjected with metallothionein-growth hormone fusion genes. *Nature* 1982, 300:611-615.
6. Palmiter RD, Norstedt G, Gelinas RE, Hammer RE, Brinster RL. Metallothionein-human GH fusion genes stimulate growth of mice. *Science* 1983, 222: 809-814.
7. Thomas KR, Capecchi MR. Site-directed mutagenesis by gene targeting in mouse embryo-derived stem cells. *Cell* 1987; 51(3):503-512.
8. Misra RP, Duncan SA. Gene targeting in the mouse. *Endocrine* Dec 2002.19(3):229-238.
9. Gulezian D, Kram DJ, McCollough B, et al. Use of transgenic animals for carcinogenicity testing: Considerations and Implications for risk assessment. *Toxicologic Pathology* 2000; 28(3):482-499.
10. Picciotto MR, Wickman K. Using knockout and transgenic mice to study neurophysiology and behaviour. *Physiological Reviews* Oct 1998;78(4):1131-1155.
11. Bowers BJ. Applications of transgenic and knockout mice in alcohol research. *Alcohol research & Health* 2000; 24(3):175-183.
12. Lim KI, Dumenco LL, Yun J. et al. High level regulated expression of the chimeric P-enolpyruvate carboxykinase gene in transgenic mice. *Cancer Res* 1990; 50:1701-1708.
13. Gossen M, Bujard H. Tight control of gene expression in mammalian cells by tetracycline-responsive promoters. *Proc. Natl Acad Sci.USA* 1992; 89:5547-5551.
14. Sauer B, Henderson N. Site specific DNA recombination in mammalian cells by the Cre recombinase of bacteriophage P1. *Proc. Natl Acad Sci. USA* 1988; 85:5166-5170.
15. Folkesson R, Winbald B, Benedikz E. Alzheimer transgenic models. *Curr Opin Psychiatry* 2002; 15:433-439.
16. Gupta SK. *Drug Screening Methods* 2004; Jaypee Publishers, New Delhi: 97-99.
17. Deltour L et al. *Journal of Biochemistry* 1999; 274:16796-16801.
18. Hodge CW, Mehmert KK, Kelley SP et al. Supersensitivity to allosteric GABA<sub>A</sub> receptor modulators and alcohol in mice lacking PKC $\alpha$ . *Nature Neuroscience* 1999;2:997-1002.
19. Powell-Braxton L, Veniant M, Latvala RD et al. A mouse model of human familial hypercholesterolemia: markedly elevated LDL and severe atherosclerosis on a low fat chow diet. *Nat Med* 1998; 4:934-938.
20. Coleman DL. Obese and diabetes, two mutant genes causing diabetes-obesity syndromes in mice. *Diabetologia* 1978; 14:141-148.
21. Peterson RG, Shaw WN, Neel M-A et al. Zucker diabetic fatty rat as a model for noninsulin-dependent diabetes mellitus. *ILAR News* 1990; 32:16-19.
22. Thurlby PL, Trayhurn P. The development of obesity in preweanling (ob/ob) mice. *Br J Nutr* 1978; 39:397-402.
23. Crofford OB, Davis CK Jr. Growth characteristics, glucose tolerance and insulin sensitivity of New Zealand Obese mice. *Metabolism* 1965; 14:271-280.
24. Ghosh MN. *Fundamentals of experimental pharmacology* 3<sup>rd</sup> edn. Hilton & Company publishers, Kolkata 2005:8-9.
25. Mockrin SC, Dzau VJ, Gross KW, Horan MJ. Transgenic animals new approaches to hypertension research. *Hypertension* 1991; 17(3):394-399.
26. Rudmann DG, Durham SK. Utilization of genetically altered animals in the Pharmaceutical industry. *Toxicologic Pathology* 1999; 27(1):111-114.
27. Srinivasan K, Ramarao P. Animal models in type-2 diabetes research: An overview. *Ind J Med Res*, mar 2007; 125:451-472.
28. Internet resource obtained from URL: <http://www.jax.org/resources/documents/imr/>
29. Internet resource obtained from URL: <http://tbase.jax.org>.

# Equity and health in India

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## I. Background

"Invest in health, build a safer future" was the theme for World Health day 2007<sup>1</sup>. There is growing realization for the fact that one of the important contributory factors for economic growth of a Nation is health of its people. India can take legitimate pride for the progress and development achieved in the recent past. It is fourth largest and second fastest growing economies in the world.<sup>22</sup> . However it does not mean that health scenario has also shown improvement proportionately.

India's population is more than 1.027 billion of which 72.22 lives in rural areas. India's Infant Mortality rate is 68 per thousand live births and maternal mortality being still high at 407 per 100,000 live births. Only 65.1 % pregnant women are attended by trained personnel during pregnancy and about 42.5 % of deliveries are attended by trained personnel.<sup>3</sup> One hospital bed is available for about 1451 population where as only one physician is available for 1916 population. Population below 15 years is 35.6 per cent and sex ratio being 933. Per capita income in 1996 was about \$310.<sup>4,5</sup> and it is expected to address issues related to universal access to equitable, affordable and quality health care and aims to achieve goals set under Millennium Development Goals (MDG). Unless India plans for equitable and efficient health care system, ensuring achieving MDG by 2015 will be distant dream.

## II. Equity and health

Equity is originally a Latin word and it means being equal or fair. Equity itself is a very broad concept and has various facets. Equity in health takes into consideration all different groups of the society with respect to opportunities in order to remain healthy. These different groups could be differentiated on the basis of economic status, religion, gender or other disadvantaged category. Equitable distribution of health services denotes responding to health needs of the poor or disadvantaged sections of population.<sup>7</sup> Other issues which need consideration for equity front of health are health financing, health care delivery system and utilization of health services.<sup>8</sup>

World Bank documents that basic determinants of health such as clean water, good sanitation make poor people more susceptible for acquiring infection. Inability to afford high quality of medical care, they often have to compromise quality of health facilities which are poor in terms of accessibility, infrastructure, supply-logistics,

prescribers' skill etc.<sup>9, 10</sup> From equity point of view, if mortality pattern of children of high and poor income countries is analyzed, it has been observed that mortality of children between high income countries continued to fall while for selected poor countries it remained the same or in fact increased between 1990-2002.<sup>11</sup> In another study it has been observed that<sup>121</sup>

- 41% of poorest quarter of world's population is underweight compared to 3 % of the richest.
- When 114 under five deaths occur among poorest quarter the corresponding figure for the richest quarter is only 13.
- Maternal mortality is 63 for poorest quarter as compared with 4 for the richest quarter

These evidences show that the concepts of equity, poverty are closely related to health and also to each other. Inequities in health and deprivations suffered by poor communities get translated into ill health. Though these figures represent data gathered from all over the globe, they are important and relevant in the context of equity and health issues for the developing country like India.

## III. Poverty and ill health

Poverty is a very complex and multi-dimensional phenomenon. It has repercussions on various aspects of life, health being one of them. Poverty makes individuals adapt to those lifestyles which may have detrimental effects on health. It may range from lack of access to safe drinking water, choosing unsafe source of water for drinking, inability to maintain inadequate sanitation resulting in unhygienic domestic conditions, inability to seek quality health services etc. The matter is further complicated by low immune status, susceptibility to malnutrition and communicable diseases.<sup>13</sup>

A wide gap has been observed in some of the critical health indicators such as infant mortality and under five mortality rates in Human Development Report (2006). The figures for richest and poorest vary between 38 to 97 and 46 and 141 respectively. Similarly percentage of births attended by skill birth personnel varies between 84 to 16 among richest and poorest population respectively.<sup>14</sup>

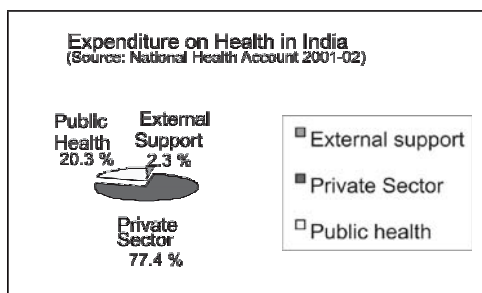
A marked difference has been documented in various studies regarding utilization of public/private health facilities by people based on their economic status. A large number of people among the lower income quintiles from the rural areas utilize public providers especially for out patient treatment compared to higher utilization of

inpatient facilities by higher quintiles.<sup>4</sup> In another case, more than 80 per cent of illness episodes treated as outpatient care requires out-of-pocket expenditure. When it comes to inpatient care, economically well-off people use disproportionately more of public sector facilities, reducing poor people's access to those facilities. The poor either resort to private sector by incurring loans or get no care at all which may be responsible for pushing families further into poverty.<sup>15</sup> Out-of-pocket (OOP) financing for health care had been also reported in other Asian countries such as Bangladesh, China, having a high prevalence of catastrophic payments and a large poverty impact of these payments. (May 2005)<sup>16</sup>

#### IV. Expenditure on health

On one hand India's has a huge and increasing population base and on the other hand expenditure on health as a percentage of GDP showed declining trend from 5.1 in year 1999 to 4.8 in 2003. The poor people are forced to seek health care from private sector at a higher cost in the absence of assessable and optimally functioning government health system or forgo the treatment altogether.<sup>17</sup> However increase in Public expenditure on Health does not necessarily mean that it would result into poverty reduction or improvement in the health indicators.<sup>18</sup> While India spends about 4.8 % of Gross Domestic Product expenditure on Health, corresponding figures for USA and UK are 15.2 % and 8 % respectively.<sup>19</sup>

Figure 1:



The government health expenditure is broadly divided in three categories:

1. Medical / curative component – Comprises of expenditure on Hospitals/ dispensaries/insurance schemes, medical education, training and other systems of medicine. (Of the total expenditure by MOHFW, a significant percentage (95.5%) was attributed to allopathic system of medicine and only 4% towards Indian system of medicine.
2. Public Health – Comprises of expenditure on prevention and control of diseases, prevention of food adulteration, drug control, minimum needs program
3. Family welfare services in urban and rural areas.

The decline in the share of central grants in the recent past

has resulted in greater impact for the poorer states compared to middle income or rich states. The greatest impact in the poor states expenditure is on their public health expenditure. This has adversely affected poor population in these states. If the same trend continues, the gap between these states will further widen because poor / marginalized population will be forced to utilize services from the private sector.

#### V. Inequities in urban vs rural settings

In India, for 72 per cent of rural area, only 33 per cent of government health resources have been allocated. In terms of per capita allocation, urban population received more than 5 times what the rural population received. This may explain the disparity between urban and rural population in terms of health indicators.

There are 2.47 lakh Panchayati Raj Institutions (PRIs) and 3682 Urban local bodies (ULBs) in India (TFC 2005). The total health expenditure of Panchayati Raj Institutions was Rs 15,281 million and that of urban local governments Rs 16,503 million.<sup>20</sup> <http://mohfw.nic.in/NHA%202001-02.pdf>

Although annual household expenditure and cost of treatment per episode for outpatient and inpatient care is higher in urban areas, expenditure as a percentage of income is higher in rural areas.<sup>21</sup>

Only 32 per cent hospitals and 22 per cent beds are in rural areas. Allopathic Doctors who are unwilling to work in rural areas dominate urban areas; thus contributing to disparities between urban and rural areas. It has been shown that higher income people in urban areas prefer to go to private hospitals as they perceive that by paying money they can get better treatment at private facilities.<sup>22</sup>

It has been said that 57% of annual deaths among

Table 1:

	BPL	IMR	U5MR	%Children undernourished
Urban	23.6	44	63.1	38.4
Rural	27.1	75	103.7	49.6
Total	26.1	70	94.9	47.0

Source: NFHS-2

underfives can be prevented through achievement of high coverage of basic health and nutrition interventions. An effective implementation of the interventions will lead to achievement of Millennium Development Goals.

#### VI. Social Aspects of Equity

Research all over the globe has shown that income inequalities predispose individuals for increased morbidity and mortalities.<sup>23</sup> In India, about 25% of population is below poverty line.<sup>24</sup> In order to achieve equitable distribution of health care in Indian context, one can not afford to ignore social dimensions. It is challenging to

address these issues because they have the roots deep seated in the socio-culture values which have been passed from one generation to other for many centuries.

### A) Religion and caste

Divisions and disparities on the basis of religion and caste had been observed all over the globe; in American continent, Africa, Europe or elsewhere in Asia. However in India it appears to be more pronounced. In fact, Indian caste system is one of the notorious examples of social division by means of subjugating certain population groups which may have effects on health outcomes. Subramanian V. et al in their study have shown that socio-economic status differentials substantially account for the health inequalities between indigenous and non-indigenous groups in India.<sup>25, 26</sup>

Indian society is characterized by its division into castes despite constitutional advances. This division is made according to a double organization, both linear and classificatory : the Jati, name which covers the social species to which one belongs from birth and the Varna, the classification which refers to functions : Brahmin (priests), Kshatriyas (warriors), Vaishya (tradesmen, salesmen and land-owners), Shudra. Religion wise breakup of population according to Census 2001 shows that there are 82% Hindus, 12.12 % Muslim, 2.34 % Christens, 1.94 Sikhs, 0.76 % Buddhists, 0.4 % Jains and rest from other religions. About 16.48 per cent of population belongs to Schedule Castes and 8.08 per cent to Schedule Tribe category.<sup>27</sup>

Report on situation of Dalits (so called lower caste people) in India indicates that untouchability is still very alive, especially in the countryside and can be seen in the segregation of housing. Dalits have their habitation a little away from the other inhabitants and are forbidden the access to the well which is the common source of water. Moreover, segregation also exists in schools, services and public places. Due to all these social disparities dalits are forced to adopt substandard lifestyle and succumb to morbidities and mortalities.<sup>28</sup>

Population of tribal communities scheduled in the constitution of India is known as Schedules Tribes (STs) STs have traditionally lived in 15 % of country's geographical areas mainly forest, hills inaccessible terrain. Thus they also

suffer from geographic and cultural exclusion. There are about 700 state specific schedule tribes recognized by constitution of India. The State policy towards tribal development aims at providing enabling framework for tribal people, focusing on livelihood opportunities, health care provision, gender equity, empowerment etc.<sup>29</sup>

It is a principal objective of NHP-2002 to evolve a policy structure which reduces these inequities and allows the disadvantaged sections of society a fairer access to public health services.

### B) Education

According to Human Development report, 2006, Highest literacy rate is observed for the state of Kerala (89.8 %), lowest being for Bihar (38.5%) Female literacy has been on rise. 61 % of India's adult literacy rate is constituted by 58% literate females as against 73.4% literate males and needs further improvement.<sup>30</sup>

According to the 2001 Population Census for India, despite the continuing gender disparity in education, gender gaps in literacy appear to be diminishing in some of the states that traditionally have had the most serious problems. Innovative attempts are being made, as in the state of Haryana, to increase girls' school attendance by providing escorts to reduce families' concern about threats to their security.

### C) Woman Reproductive health and reproductive rights

#### C.1) Gender

A momentum for addressing equity related gender issues, women's reproductive rights was created by International conference on population and development at Cairo Conference in 1994 following which many countries have incorporated gender perspective in their policies/ programmes and activities.<sup>31</sup> UNFPA endorses the fact that gender equality and women's empowerment are essential to achieving reproductive health and sustainable development. The costs of gender discrimination are highest for low-income countries, and within countries, for the poor because women constitute a large share of the labor force and play a central role in rural economies and food production. They are also primary guardians of the next generation.<sup>32, 33</sup>

In large parts of the developing world, traditions and socio-cultural norms still trap countries in poverty as they bar women from economic activities: more discrimination – less economic growth – more poverty. To address these issues, Organization for Economic Cooperation and Development (OECD) which is active in 30 countries, helps governments to take into account gender equality in development of policies.<sup>34,34</sup> <http://www.oecd.org/dataoecd/44/56/37962700.pdf>

Unmarried adolescent abortion-seekers reported a markedly higher use of traditional providers than married women, despite the availability of other abortion services. Unsafe abortion is closely associated with poverty, social

### Differentials in Health status Among Socio-Economic Groups

Indicator	Infant Mortality /1000	Under 5 Mortality /1000	% Children Under weight
India	70	94.9	47
Social Inequity			
Scheduled Castes	83	119.3	53.5
Scheduled Tribes	84.2	126.6	55.9
Other Disadvantaged	76	103.1	47.3
Others	61.8	82.6	41.1

Source: National Health Policy 2002

inequity, and the persistent, systematic denial of women's human rights.<sup>35</sup> However State of world population (2004) reports that some programmatic interventions have been successful in India to educate women about reproductive and human rights; others offer training in literacy, employment skills, legal rights, parenting, child health, and social mobilization.<sup>36</sup>

### **C.2) Sex Ratio**

The sex ratio (number of females per 1000 males) has been steadily declining in India. From 1901 to 2001, the sex ratio has declined from 972 to 933, highest being in Kerala (1058). This is largely attributed to sex selective abortions (female foeticides) due to the son preference and discrimination against the girl child, leading to higher mortality levels for females in every stage of life of a female. Punjab and Haryana which represent richest states of India, have sex ratio 874 and 861 respectively. This indicates that improvement in economic status may not go hand in hand with the improvement in gender related issues. Studies have established correlation between low sex ratio and high maternal mortality has been established.<sup>37</sup>

### **C.3) Status of woman**

India has a male dominated society. Therefore Life cycle approach of Indian females shows discrimination and disparities at each stage of her life. Strong socio-cultural influences on status of women make them susceptible to morbidities and mortalities. Predominantly it is due to the fact that Indian societies have strong preference for sons compared to daughters. A married female is expected to undergo risks of repeated pregnancies till she delivers a male child. Percentage of women with two daughters and no sons and want no more children, is increasing from 47% in NFHS-2 to 62% in NFHS-3.<sup>38</sup> There exist biases for upbringing of male and female children which may be in terms of duration of breast feeding, distribution of food, immunization, education/ schooling opportunities, health care seeking behavior etc.

***"Empowered women can be some of the most effective rivers of development."***

***- UN Secretary-General Kofi Annan***

### **C.4) Domestic Violence Widespread**

Inequity in the status of male and female in the society is evident from NFHS 3 findings that 52.5% of currently married women in India participate in household decisions where as 62.8 % of ever married women have experienced spousal violence.<sup>39</sup> A substantial proportion of married women have been reporting physical or sexual abuse by their husbands at some time in their lives. Overall, 37% of women report abuse, with large variations among the states.

### **C.5) Decision Making**

There are some issues which influence decision making while availing health services. In the context of reproductive health of a woman, safe motherhood has

been high on the agenda for nearly two decades, but it still needs attention. For example, though age of marriage is 18 years as defined by the law, NHFS 3 (2005-06) reports that forty-five percent of women (ages 20-24), were married before 18 years of age.

Despite having a higher level of education, young married women in the abortion study had a lower status in the household than older women. Younger women had significantly lower decision-making powers, less mobility and less likelihood of having an independent source of income or control over money earned. These factors affect decision making process for abortion.<sup>40</sup>

In the year 2004, only about 5 % of total women of India occupy seats in lower house. (HDR 2006) Women continue to be grossly under-represented in positions of power and decision-making, because of obstacles such as poverty, illiteracy and limited access to education, inadequate financial resources, patriarchal mentality and the dual burden of domestic tasks and occupational obligations.<sup>41</sup>

## **VII. Discussion and Conclusion**

Several evidences suggest that the health needs of the poor are still overlooked. According to Human Development Report 2006, only about one third of population of India had sustainable access to improved sanitation in 2004.<sup>42</sup>

Those with access to health facilities are usually members of upper social strata who already have better access to better care. Inverse association between geographically available health resources and measures of population need for health care is well established.<sup>43</sup> Both government and private expenditures on health are higher for higher income quintiles and for people living in urban areas and working in organized sector. Delivery of health care is found to be biased for urban areas. It has also been shown that people in lower income quintile and rural areas bear higher burden of health expenditures a proportion of their income. For 82 percent of illness episodes, in rural areas and 79 per cent in urban areas, people go to private provider.<sup>4, 44</sup>

Studies on out of pocket payments, in Asian countries showed, Bangladesh, China, India, Nepal and Vietnam rely mostly heavily on OOP financing and have heaviest incidence of catastrophic payments (severely disrupting household living standards).<sup>45</sup>

For understanding various issues related to equity related to health in Indian context, a conceptual framework has been developed.

Efforts for achieving equitable societies will not only help reducing health inequities building health status of all sections of population but also expand the opportunities for all, which will result in better use of resources and contribute to the productivity, sustainable economic development of India.

## **X. References**

1. World Health Organization <http://www.euro.who.int/>

- eprise/main/WHO/Progs/whd07
2. [http://en.wikipedia.org/wiki/Economy\\_of\\_India](http://en.wikipedia.org/wiki/Economy_of_India)
  3. Census India 2001
  4. Garg Cahru C. Equity of health sector financing and delivery in India June 1998.
  5. <http://equitableindia.org/>
  6. National Rural Health Mission. (2005). National Rural Health Mission Document (2005-2012) New Delhi: Retrieved in 2006, from [www.hoffw.nic.in /NRHM/20Mission/20 Document.pdf](http://www.hoffw.nic.in/NRHM/20Mission/20Document.pdf)
  7. Whitehead M. The concepts and principles of equity in health. *Int J Health Ser* 1992;22:429-445. Health Policy and development Vol 2, No.3 Dec 2004.
  8. Braveman Paula and Gruskin Sofia. "Poverty, equity, Human rights and health" *Bulletin of World health Organization* 2003, 81 (7) 539-545.
  9. <http://web.worldbank.org/wbsite/external/topics/extpoverty/extprs/0,contentMDK:20177542-pagePK:148956-piPK:216618-the sitePK:384201,00.html>
  10. Victora C.G., Vagstaff A, Schillenberg JA, Gwatkin D, Claeson C, Habicht JP Applying an equity lens to child health and mortality: more of the same is not enough. *Lancet* 2003;362:233-41
  11. Jamison D, et al. *Priorities in Health*. Washington , D.C.: World Bank 2006a. <http://www.globalforumhealth.org/filesupld/forum9/CD%20Forum%209/papers/Shetty%20P.pdf>
  13. WHO: "Poverty Reduction Status Papers: Their Significance for Health": second synthesis report; 2004. <http://www.who.int/hdp/en/prsp.pdf>
  14. Human Development Report 2006 [http://hdr.undp.org/hdr2006/statistics/countries/data\\_sheets/cty\\_ds\\_IND.html](http://hdr.undp.org/hdr2006/statistics/countries/data_sheets/cty_ds_IND.html)
  15. Murthy Nirmala Health, Gender and Poverty: Evidence, Issues and Solutions <http://www.dhan.org/news/docs/Health,%20gender%20and%20poverty.doc>
  16. <http://www.equitap.org/publications/wps/EquitapWP2.pdf>
  17. [http://www.who.int/whr/2006/whr06\\_en.pdf](http://www.who.int/whr/2006/whr06_en.pdf)
  18. Dollar D, Kraay A. Growth is good for poor. Washington D.C.: World Bank; 2000.
  19. World health Report 2006. [http://www.who.int/whr/2006/annex/06\\_annex2\\_en.pdf](http://www.who.int/whr/2006/annex/06_annex2_en.pdf)
  20. <http://mohfw.nic.in/NHA%202001-02.pdf>
  21. Shariff, A. (1995) "Health transaction in India", National Council of Applied Research, New Delhi. Working paper no. 57. <http://www.hsph.harvard.edu/takemi/rp144.pdf>
  23. John W Lynch, Davey Smith George, Kaplan House A, George James S. "Income inequality and mortality: importance to health of individual income, psychosocial environment, or material conditions" *BMJ* 2000;320(7243):1200 doi:10.1136/bmj.320.7243.1200
  24. 2007 Cia World Factbook, India Economy - 2007 [http://www.theodora.com/wfbcurrent/india/india\\_economy.html](http://www.theodora.com/wfbcurrent/india/india_economy.html)
  25. Subramanian SV, Smith GD, Subramanyam M (2006) Indigenous Health and Socioeconomic Status in India. *PLoS Med* 3(10): e421 doi:10.1371/journal.pmed.0030421
  26. Subramanian S.V., Nandy Shailen, Irving Michelle, Gordon Dave, Lambert Helen, Davey Smith George. "The Mortality Divide in India: The Differential Contributions of Gender, Caste, and Standard of Living Across the Life Course." *AJPH* 2006, Vol 96, No. 5 : 818-825 doi: 10.2105/ajph.2004.060103
  27. <http://www.censusindia.net/results>
  28. [http://indianhope.free.fr/site\\_eng/dalit.php3](http://indianhope.free.fr/site_eng/dalit.php3)
  29. The National Draft policy, Ministry of Tribal affairs. <http://tribal.nic.in/finalContent.pdf>
  30. Human Development Report 2006 [http://hdr.undp.org/hdr2006/statistics/countries/data\\_sheets/cty\\_ds\\_IND.html](http://hdr.undp.org/hdr2006/statistics/countries/data_sheets/cty_ds_IND.html)
  31. United Nations. Report of the International Conference on Population and Development, Cairo, 5—13 September 1994. Document A/CONF. 171/13/Rev. 1. New York: United Nations; 1995.
  32. State of world Population: Gender Equality and Women's Empowerment. <http://www.unfpa.org/swp/2004/english/ch5/index.htm>
  33. [http://www.undp.org/execbrd/word/UNFPA %20document%20on%20gender%20mainstreaming.doc](http://www.undp.org/execbrd/word/UNFPA%20document%20on%20gender%20mainstreaming.doc)
  35. Gasman N., Blandon M.M., Crane B.B. "Fulfilling Women's Reproductive Intentions. Abortion, social inequity, and women's health: Obstetrician-gynecologists as agents of change Behavior". *International Journal of Gynecology and Obstetrics* (2006)94 310—316
  36. State of world Population: Gender Equality and Women's Empowerment <http://www.unfpa.org/swp/2004/english/ch5/index.htm>
  37. Coale, Excess female mortality and the balance of Sexes in Population: An estimate on number of missing Females, *Population and development review*, Vol. 17 (3), 1991.
  38. National family health Survey <http://nfhsindia.org/summary.html>
  39. <http://www.nfhsindia.org/pdf/IN.pdf>
  40. Ganatra Bela, Hirve S.S. "Induced abortions: decision-making, provider choice and morbidity experience among rural adolescents in India" [http://www.who.int/reproductive-health/publications/towards\\_adulthood/21.pdf](http://www.who.int/reproductive-health/publications/towards_adulthood/21.pdf)
  41. Report of the International Forum for the Operational Review and Appraisal of the Implementation of the Programme of Action of the International Conference on Population and Development (ICPD): "Enhancing gender equality, equity and empowerment of women" 1999
  43. Gwatkin DR, Bhuia A, Victora CG. Making health systems more equitable. *Lancet* 2004; 364: 1273-80
  44. Berman P. A. (1997): "Rethinking Health Care Systems: Private Care Provision in India" *Harvard School of Public Health*, July

45. Doorslaer Eddy van, O'donnell Owen, P Ravindra Rannan-Eliya, Somanathan Aparnaa, Adhikari Shiva Raj, Garg Charu C, Harbianto Deni, Herrin Alejandro N, Huq Mohammed Nazmul, Ibragimova Shamsia, Karan Anup, Lee Tae-Jin, Leung Gabriel M Jui-Fen

Rachel Lu Chiu Wan Ng, Pande Badri Raj, Racelis Rachel, Tao Sihai, Tin Keith, Tisayaticom Kanjana, Trisnantoro Laksono, Vasavid Chitpranee, Zhao Yuxin : Catastrophic payments for health care in Asia. Health Econ. 2007 Feb 21; : 17311356

# Axillary filarial swelling: A case study

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## Introduction

Lymphatic filariasis is a major health problem in many parts of India, usually being endemic in those areas. In these endemic areas filariasis is a major cause of morbidity and disfigurement in these areas although the majority of the cases being asymptomatic. The disease manifestation of the lower limb lymphoedema, hydrocele, chyluria or rarely groin lymphadenovariex is due to progressive lymphatic dysfunction and dilation [1, 2]. Axillary lymphadenovariex is an extremely uncommon presentation of filariasis, especially in the presence of peripheral eosinophilia and absence of peripheral microfilaria especially after diethylcarbamazine (DEC) challenge test [3].

## Case report

16 year old Hindu male in July 2010 presented complaining of swelling 1×1 cm in the right anterior axillary fold. The swelling was painless, mobile, and 5-6 month duration. He was a manual labourer and often visited Bihar (a region endemic for filariasis). He had no history of cough fever and weight loss or any other swelling in the body, clinical examination of the swelling revealed a 1×1 cm mass, painless, mobile, and cystic in consistency in the right anterior axillary fold. No other swelling lymph node or lump was noted anywhere else. The provisional Diagnosis of lymphadenopathy under investigation was given. and investigation involving CBC, X-Ray Chest, USG axilla and FNAC were done.

CBC was unremarkable other than for peripheral eosinophilia, X- Chest was unremarkable. USG revealed a cystic anechoic thin walled rounded structure 1×1 cm in the right anterior axillary fold, no internal septae or debris were noted. FNAC led to aspiration of few drops of fluid following which the swelling subsided but reappeared after 4-5 days. The Geimsa stain of the fluid revealed

multiple microfilaria of *Wuchereria bancrofti* in a background of pus cells. The patient was given a 3 week course of DEC (100mg 8 hourly), following which the swelling reduced considerably. In September 2010, a repeat USG was done to confirm the finding and the swelling was found to reduce to 0.5×0.5 cm and an ultrasound guided FNAC failed to extract any fluid. The patient had no other sign and symptom attributable to filariasis. No scrotal nodule developed during the course of treatment nor there was any sign of oedema of lower limb. DEC challenge was again done and it came out to be negative for any microfilaria.

## Discussion

Lymphatic filariasis is a major health problem in India with most infections caused by *Wuchereria bancrofti*. The presence of adult worms of *Wuchereria bancrofti* in the infected individuals is confirmed by detecting microfilariae or filarial antigens in the patient's blood [4]. Ultrasound scans (B-mode and M-mode) with or without colour Doppler or pulse wave Doppler have been used to detect living adult *W. bancrofti* (filarial dance sign) in dilated intrascrotal juxtatesticular lymphatics (worm nests) of approximately 80% of microfilaremic but asymptomatic men residing in endemic areas [5]. In individuals from endemic regions, with no sonologically detectable worms or microfilaremia, the presence of dilated lymphatics in the scrotum has been shown to be due to occult adult worms in those lymphatics [1]; treatment with diethylcarbamazine has led to the formation of scrotal nodules, histological examination revealing dead adult worms [4]. To the best of our knowledge there are no reports of FNAC aspirates of axillary nodule showing microfilariae on microscopy in the absence of detectable worm or dilated lymphatics. The diagnosis of a filarial infection can also be made by detecting microfilariae on microscopic examination of fine needle aspirates from lymph nodes [6, 7]. Fine needle aspiration cytology from breast mass, thyroid mass, hydrocoele fluid, pericardial fluid, pleural fluid, ascitic fluid, and cytology of cervicovaginal smears, bronchial aspirates, urine, nipple secretion, bone marrow and joint fluid aspirates have also been reported to yield microfilariae [8,9]. Moreover, in these patients the peripheral smears rarely revealed microfilaremia or eosinophilia [8, 9].

This case of filariasis is different and unique from other cases due to certain reasons. Firstly, although the filarial lymphangiectasia presenting as visible lump

**Fig 1:** Microfilaria in FNAC





(lymphadenovarix) is rare, in our case there was no lymphadenovarix just a solitary mobile nodule. Secondly the Ultrasound of the axilla didn't reveal any living or dead worm in the nodule, however the absence of worms in the lymphatics on the ultrasound does not, however, rule out their presence in the deeper lymphatics of the axilla [10]. Thirdly the microfilaria disappeared upon treatment with diethylcarbamazine which was evidenced by absence of microfilaria upon ultrasound guided FNAC. Moreover the swelling regressed following treatment with Diethylcarbamazine.

## Conclusion

Lymphatics of the lower limbs, scrotum are the preferred location for adult *W. bancrofti*, axillary lymphatics, although rare can also be affected and even in some exceptional cases the worms can present as a nodule without lymphatic involvement as in our case. The host-parasite interaction in these lymphatics may be different from those in lymphatics of limbs and scrotum. This may explain the formation of a lymphadenovarix in the axilla or the presence of solitary nodule in axilla and also the dramatic response to diethylcarbamazine.

## References

1. Dreyer G, Addiss D, Roberts J, Noroes J: Progression of lymphatic vessel dilatation in the presence of living adult *Wuchereria bancrofti*. *Trans R Soc Trop Med Hyg* 2002 , 96:157-161. PubMed Abstract | Publisher Full Text.
2. Sen SB, Chatterjee H, Ramaprasad S: Chylous manifestations of filariasis: A clinical and lymphographic study. Part II. Lymphadenovarix, chylocele and chylous scrotum. *Ind Jour Med Res* 1969 , 57:1738-1744.
3. Adish Basu, Sarath Chandra Sistia, Surendra Kumar Verma: Lymphadenovarix in axilla – an unusual presentation of of Filariasis. *Filaria Journal* 2006, 5:9doi:10.1186/1475-2883-5-9
4. Dreyer G, Santos A, Noroes J, Addiss D: Proposed panel of diagnostic criteria, including the use of ultrasound, to refine the concept of 'endemic normals' in lymphatic filariasis. *Tropical Medicine and International Health* 1999 , 4:575-579. Publisher Full Text
5. Noroes J, Addiss D, Amaral F, Coutinho A, Medeiros Z, Dreyer G: Occurrence of adult *Wuchereria bancrofti* in the scrotal area of men with microfilaremia. *Trans R Soc Trop Med Hyg* 1996 , 90:55-56. PubMed Abstract | Publisher Full Text
6. Dey P, Radhika S, Jain A: Microfilariae of *Wuchereria bancrofti* in a lymph node aspirate. A case report. *Acta Cytol* 1993 , 37:745-746. PubMed Abstract
7. Kapila K, Verma K: Diagnosis of parasites in fine needle breast aspirates. *Acta Cytol* 1996 , 40:653-656. PubMed Abstract
8. Varghese TR, Raghuvver CV, Pai MR, Bansal R: Microfilariae in Cytologic Smears. A Report of Six Cases. *Acta Cytol* 1996 , 40:299-301. PubMed Abstract
9. Walter A, Hemalatha K, Cariappa A: Microfilariae of *Wuchereria bancrofti* in cytologic smears. *Acta Cytol* 1983 , 4:432-436.
10. Reddy GS, Das LK, Pani SP: The preferential site of adult *Wuchereria bancrofti*: an ultrasound study of male asymptomatic microfilaria carriers in Pondicherry, India. *Natl Med J India* 2004 , 17:195-196. PubMed Abstract.

# Prevalence and risk factors of type – 2 diabetes mellitus in Kadapa urban population aged 30 years and above

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## Intruduction

Diabetes Mellitus, long back considered a disease of minor significance to World Health, is now emerging as one of the main threats to human health in the 21<sup>st</sup> century<sup>1</sup>. The past two decades have seen an explosive increase in the number of people diagnosed with diabetes worldwide. The world health organization (WHO) estimated that there were 135 million diabetics in 1995 and this number would increase to 300 million by the year 2025. The prevalence of diabetes is steadily increasing worldwide particularly in the developing countries. There were an estimated 84 million persons with diabetes in the developing world in 1995. The Indian subcontinent accounted for a quarter of them, this number is likely to increase three folds to 226 million by the year 2025.<sup>2</sup> India currently has the world largest diabetic population with an estimated 19.4 million people. This is expected to be 57.2 million by 2025. Hyderabad is the diabetic capital of the country with every sixth person being diabetic<sup>3</sup> prevalence 16.6%.

Type 2 Diabetes mellitus is the commonest form of diabetes seen worldwide. This form of diabetes is considered as life style disease. The underlying genetic predisposition gets unmasked in the presence of the environmental factors such as sedentary life style, change in traditional food habits from coarse simple meals to highly refined caloric dense food, large amount of carbohydrate consumption and stress of urban living.

The prevalence of diabetes mellitus may vary from place to place and region to region. In the 1970s, the prevalence of diabetes among urban individuals was reported to be 2.1 percent and this has now risen to 12.1 percent. Moreover, there is an equally large pool of individuals with impaired glucose tolerance (IGT), many of whom will develop type 2 diabetes mellitus in the future.

Diabetes is now considered a vascular disease. Diabetes affects large blood vessels (cardiac, cerebral and peripheral arteries) small vessels (kidney and retina), nerves and other organs. Micro vascular and macro vascular diseases cause considerable mortality and morbidity among diabetics.<sup>4</sup> Diabetes can affect nearly every organ system in the body, it can cause blindness, lead to end stage renal disease, lower extremity amputations, and increased the risk for stroke, ischemic heart disease, peripheral vascular disease and neuropathy. This is causing great concern since the cost of treating diabetes is becoming a serious drain on health resources.<sup>5</sup> in type 2 diabetes mellitus the risk of

some of these complications (eg. coronary artery disease), may start even before the onset of diabetes. Diabetes are 25 times more likely to develop blindness, 17 times more likely to develop kidney disease, 30-40 times likely to undergo a major amputation, 2 – 4 times chances of developing myocardial infarction and two times chance of stroke with diabetes<sup>6,7,8</sup>. It is estimated that during 1997 about 1, 02,000 persons died of diabetes mellitus in India with about, 19, 81,000 Daly's lost.

Diabetes mellitus exhibits the Iceberg phenomenon, where the unknown morbidity exceeds the known morbidity. The diagnosis is established either during a routine health checks up or when the patient presents with complications. Several factors have been implicated in the etiology of diabetes mellitus. These include geographic, ethnic considerations, genetic, socio economic, socio cultural and dietary patterns, nutritional status, sex and biological agents. In addition diseases like pancreatitis, Cushing's syndrome and hyperthyroidism are also known to cause diabetes mellitus. In many extensive studies no single factor has been identified in the causation. Diabetes mellitus causes enormous damage to the self and social usefulness of the individual, and to the country in terms of loss of effective manpower, and increased expenditure on country resources.

In order to throw more light on this matter, an attempt is being made to study the prevalence and risk factors of type 2 Diabetes mellitus among the 30 yrs and above age group, in the urban field practice area of Rajiv Gandhi Institute of Medical Sciences (RIMS), Kadapa. Simple life style modifications will change the epidemic scenario. Prevention of Diabetes mellitus or delay in onset of diabetes mellitus even in a single patient represents a triumph to the health care system and national economy.

## Objectives

1. To know the prevalence of type 2 Diabetes in urban areas of Kadapa.
2. To find the risk factors associated with Diabetes Mellitus.

## Material & methods

The present community based cross sectional study was carried out in the urban health centre area Akkayapalli, Kadapa for a period of one year from April 2009 to March 2010 (including analysis and conclusions). Urban Health

Centre, Akkayapalli covers about the population of 25,152 with two sub centres. First sub centre is having 8 hamlets and second sub centre is having 7 hamlets. In this study "Systematic random sampling" method was used.

In each habitation first reached the centre of the area, there selected the one of the lane by lottery based after giving the lanes number. If the random number is 3, then the survey started from the 3<sup>rd</sup> house onwards. Similarly 3<sup>rd</sup>, 13th, 23<sup>rd</sup> house and so on till I get the required sample. In one house we got 3 eligible age group persons then taken the history of all the three persons. Suppose there is no eligible age group persons of >30 yrs of age, then moved to the another house.

### Calculation of sample size

Sample size for this study can be drawn from prevalence of diabetes mellitus on Hyderabad urban population published in Indian journal of medical research March 2003 article by ICMR.

In this study prevalence was shown to be 16.7%, and allowable error taken as 15% and formulae<sup>13</sup> used here is  $4PQ / L^2$ .

Where, P = prevalence of diabetes mellitus (16.6%)

Q = 100 – P

L = Allowable error (15%)

According to the above formulae, sample arrived was 754. A proforma was designed and approval was taken from the faculty and head of the department of community medicine, RIMS Medical College, Kadapa.

### Definition

A patient or person described as suffering from diabetes mellitus, if he had been diagnosed by the physician or qualified doctor or was on treatment for diabetes. In the study population, whose fasting blood sugar  $\geq 126$  mg/dl with symptoms was considered to be diabetic patient as per the recently modified diagnostic criteria <sup>11</sup>(ADA).

### Procedure

Biochemical test that is fasting blood sugar test was done in community which belonging to Urban Health Centre, Akkayapalli. For measuring fasting blood glucose, Accu check glucometer (Boeringer Mannheim) was used. One day before visited the concerned cluster and ask them to stay and keep them under fasting state. The index finger was cleaned, dried and pricked with a sterilized pricker. Blood was allowed to collect, the first few drops were wiped off gently after which the glucose strip was inserted and the reading was noted. The data was analyzed and necessary statistical application

### Results

The present study was conducted on 754 individuals selected in Urban Health Centre area by Systematic random sampling method and examined over a period of one year. Of these,

Prevalence of diabetes mellitus in the study population was 11.4% on the other hand impaired glucose tolerance

**Table 1:** Prevalence of diabetes mellitus in the study population

Among Study Population	No of cases	Prevalence per 100 study population
Diabetes Mellitus	86	11.4%
IGT	97	12.8%
Normal people	571	75.8%
Total	754	100%

IGT=Impaired glucose tolerance.

people were also increasing and was found to be 12.8% and normal people was 75.8% in the present study.

The above table shows that there was a gradual increase in prevalence of diabetes mellitus from 30 yrs onwards, with maximum prevalence (16.1%) was noticed between 51-60yrs of age after which it declines as the age advances. The observed difference in occurrence of diabetes mellitus between the different age groups was statistically

**Table 2:** Age wise distribution of diabetes mellitus

Age	DM present		DM absent		Total	
	No	%	No	%	No	%
30 – 40	21	(6.8)	284	(93.2)	305	(100)
41 – 50	27	(12.7)	184	(87.3)	211	(100)
51 – 60	18	(16.1)	94	(83.9)	112	(100)
$\geq 61$	20	(15.8)	106	(84.2)	126	(100)
Total	86	(11.4)	668	(88.6)	754	(100)

$X^2$  11.47, 3df, P<0.001

significant (p < 0.001) and was not due to chance.

In the study population 14.5% prevalence of diabetes mellitus among males and 10.1% prevalence of diabetes mellitus among females. But, out of 86 diabetics 30.0% were males and 70.0% were females. In the non-diabetic population (out of 668), 29.9% were males and 70.1% were females.

**Table 3:** Sex wise distribution of diabetes mellitus

Sex	DM present		DM absent		Total	
	No	%	No	%	No	%
Male	34	(14.5)	201	(85.5)	235	(100)
Female	52	(10.1)	467	(89.9)	519	(100)
Total	86	(11.4)	668	(88.6)	754	(100)

The observed difference between the males and females was not statistically significant (P > 0.05).

Consumer price index in the year 2003 in an average is 496 and this was used to update the B.G. Prasad classification and divided into 5 classes.

In the present study, about 24.6% of diabetics belonging to upper class, 15% were upper middle class, 7.8% were belonging to lower middle class, 11% were from upper lower class and lastly 4% belonging to lower class.

This was divided into upper middle and upper class verses

**Table 4:** Diabetes mellitus according to per capita income (bg prasad classification)

Per capita income per month	DM present		DM absent		Total	
	No	%	No	%	No	%
>2245	18	(24.6)	55	(75.4)	73	(100)
1223-2444	31	(15)	175	(85)	206	(100)
734-1222	21	(7.8)	248	(92.2)	269	(100)
367-733	12	(11)	96	(89)	108	(100)
<366	4	(4)	94	(96)	98	(100)
Total	86	(11.4)	668	(88.6)	754	(100)

$X^2=24.05$ , 4df, P, 0.01.

other socio economic class. The observed difference between these two and diabetes mellitus was statistically significant (P < 0.001)

High socioeconomic status significantly associated with Diabetes Mellitus.

In the study population, about 19.6% diabetics from sedentary activity, 9.1% were from moderate activity and only 6.9% diabetics from severe activity.

Among diabetics (Out of 86 diabetics), 47.7% were from sedentary activity, 35% were from moderate activity and only 17.3% from severe activity.

**Table 5:** Diabetes mellitus in relation to physical activity

Physical Activity	DM present		DM absent		Total	
	No	%	No	%	No	%
Sedentary	41	(19.6)	168	(80.4)	209	(100)
Moderate	30	(9.1)	298	(90.9)	328	(100)
Severe	15	(6.9)	202	(83.1)	217	(100)
Total	86	(11.4)	668	(88.6)	754	(100)

$X^2=19.94$ , 2df, P<0.001.

Among non-diabetics (Out of 668 non diabetics), 25.1% were from sedentary activity, 44.6% were from moderate activity and only 30.3% were from severe activity.

However there is considerable difference in the sedentary, moderate and severe physical activity and this finding was statistically significant (P < 0.001)

In the study population 35.8% (270) were smokers and 64.2% (484) were non-smokers.

Among the smokers, the Prevalence of Diabetes was 19.2% and non smokers the Prevalence of Diabetes was 7.0%.

Among the Diabetics (Out of 86), 52 (60.4%) were smokers and 34 (39.6%) were non-smokers.

In the non-diabetic population, about 218 (32.6%) were smokers and 450 (67.4%) were non-smokers.

**Table 6:** Magnitude of smoking and diabetes mellitus

Smoking	DM Present		DM Absent		Total	
	No	%	No	%	No	%
Yes	52	(19.2)	218	(80.8)	270	(100)
No	34	(7.0)	450	(93.0)	484	(100)
Total	86	(11.4)	668	(88.6)	754	(100)

$X^2=25.67$ , 1df, P<0.001

The magnitude of smoking and Diabetes Mellitus was statistically significant ( P<0.001)

In the study population 27.1% (205) were consumed alcohol and 72.9% (499) were non-alcoholics.

Among the Alcoholics, the Prevalence of Diabetes was 26.3% and non alcoholic persons the Prevalence of Diabetes was 6.4%.

Among the Diabetics (Out of 86), 54 (62.7%) were

**Table 7:** Alcohol consumption and diabetes

Alcohol Consumption	DM present		DM absent		Total	
	No	%	No	%	No	%
Yes	54	(26.3)	151	(73.7)	205	(100)
No	32	(6.4)	467	(94.6)	499	(100)
Total	86	(11.4)	668	(88.6)	754	(100)

$X^2=53.81$ , 1df, P<0.01.

consumed alcohol and 32 (37.3%) were non-alcoholic persons.

In the non-diabetic population, about 151 (22.6%) were consumed alcohol and 467 (77.4%) were non-alcoholic persons.

Significant association was found between the alcohol consumption and Diabetes mellitus. (P<0.001)

In the study population 230 (30.5%) were practicing exercise and about 524 (69.5%) were not practicing any kind of exercise.

Among diabetics (86), 17 (19.7%) diabetics were practicing exercise and only remaining 69 (80.3%) were not practicing any exercise.

In non-diabetic population (668), About 213 (31.8%) were practicing exercise and about 455 (68.2%) were not practicing any exercise.

**Table 8:** Practice of exercise and diabetes mellitus

Practice of exercise	DM present		DM absent		Total	
	No	%	No	%	No	%
Yes	17	(7.4)	213	(92.6)	230	(100)
No	69	(13.2)	455	(86.8)	524	(100)
Total	86	(11.4)	668	(88.6)	754	(100)

$X^2=5.28$ , 1df, P<0.02

There appeared to be considerable difference in the prevalence of Diabetes among persons who are practicing and not practicing exercise and this association was statistically significant. (  $p < 0.05$  )

The above table shows about the Prevalence of Diabetes in the group of BMI  $< 18.5$  was 8.1%, BMI range between 18.5 to 25 was 9.0%, Prevalence of Diabetes was more in the BMI range of 25-30 was 18.5 and lastly diabetic Prevalence was in the BMI range of 30 plus was about 20.5%.

**Table 9:** Body mass index (bmi) and diabetes

BMI	DM present		DM Absent		Total	
	No	%	No	%	No	%
$< 18.5$	15	(8.1)	171	(91.9)	186	100%
18.5 – 24.99	35	(9.0)	350	(91)	385	100%
25 – 29.99	15	(18.5)	66	(91.5)	81	100%
$30 \geq$	21	(20.5)	81	(79.5)	102	100%
Total	86	(11.4)	668	(88.6)	754	100%

$\chi^2$ - 16.66, 3df,  $P < 0.005$ .

Where as in Diabetic population (Out of 86), less than 25 BMI range was about 50(58.1%) and BMI range above 25 was 36 (41.9%).

In Non Diabetic population (Out of 668), 521 (77.9%) were having BMI less than 25 and only 147 (22.3%) were having BMI more than 25.

The observed difference between the BMI range and diabetes mellitus was highly statistically significant and the finding was due to high BMI and not due to chance ( $P < 0.001$ )

Diabetes increases with increasing BMI.

Out of 86 diabetics, 30 (34.8%) people were giving father having Diabetes, about 16 (18.6%) were giving history of Mother having Diabetes and lastly 40 (46.5%) people were giving both parents having Diabetes Mellitus.

In the non diabetic population, 220 (32.9%) were giving history of father having Diabetes. About 210 (31.4%) was

**Table 10:** Family history of diseases and diabetes mellitus

Family history	DM present		DM absent		Total	
	No	%	No	%	No	%
Father Having DM	30	(11.2)	220	(88.8)	250	(100)
Mother Having DM	16	(8.)	210	(91.4)	232	(100)
Both Having DM	40	(1)	240	(86.1)	274	(100)
Total	86	(11.4)	668	(88.6)	754	(100)

$\chi^2$ -6.59, 2df,  $P < 0.05$

giving history of mother having Diabetes and lastly 240 (35.9%) were giving history of both parents having Diabetes.

Multivariate analysis was used and the observed difference

between the diabetes mellitus and other family history of disease was statistically significant ( $P < 0.001$ )

Among diabetic males, 20 (58.8%) people were showing more than or equal to 94 cms waist circumference and 14 (41.2%) people were showing less than or equal to 94 cms waist circumference.

Among non-diabetic males, 64 (31.8%) people were showing more than or equal to 94 cms and 137 (68.2%)

**Table 11:** Waist circumference of males and diabetes (n-235)

Waist circumference	DM present		DM Absent		Total	
	No	%	No	%	No	%
$\geq 94$	20	(23.8)	64	(76.2)	84	(100)
$< 94$	14	(9.2)	137	(90.8)	151	(100)
Total	34	(14.4)	201	(85.6)	235	(100)

$\chi^2$ - 9.22, 1df,  $P < 0.001$

were showing less than or equal to 94 cms of waist circumference

The observed difference between waist circumference of males and diabetes mellitus was statistically significant ( $P - 0.001$ )

Among diabetic females, 36 (69.2%) people were showing more than or equal to 94 cm waist circumference and 16 (30.8%) people were showing less than or equal to 94 cms waist circumference.

Among non-diabetic females, 160 (34.3%) people were showing more than or equal to 94 cm and 307 (65.7%) were

**Table 12:** Waist circumference of females and dm (n-519)

Waist circumference	DM present		DM Absent		Total	
	No	%	No	%	No	%
$> 80$ cm	36	(18.4)	160	(85.6)	196	(100)
$< 80$ cm	16	(5)	307	(95)	323	(100)
Total	52	(10)	467	(90)	519	(100)

$\chi^2$ - 24.34, 1df,  $P < 0.001$

showing less than or equal to 94 cms of waist circumference

The observed difference between waist circumference of females and diabetes mellitus was statistically significant ( $P < 0.001$ )

Fasting lipid profile test was done only to the diabetic individuals to know the dyslipidaemic condition (to reduce the cost).

Out of 86 Diabetic individuals, about 59 (68.6%) people were showing the dyslipidaemic condition and only less proportion of people 29 (33.4%) were showing normal eulipidaemic condition.

## Discussion

**Table 13:** Lipid profile status and diabetes mellitus:

Lipid profile status	Diabetes people	Percentage (%)
Dyslipidaemia	59	68.6%
Eulipidaemia(Normal)	29	31.4%
Total	86	100%

The present study was conducted at the urban health centre Akkayapalli, urban community of Kadapa during the period of one year from April 2009 to March 2010. A total of 754 study population were examined of whom 86 (11.4%) were found to be diabetes mellitus and 57 (12.8%) were found to be impaired glucose tolerance group.

The prevalence of the diabetes mellitus in the present study was 11.4% and similar finding was observed with Ramachandran A, Snehalatha C et al<sup>3</sup> found the prevalence was 16.6% in Hyderabad. Ramachandran A et al<sup>20</sup> (2002) the prevalence was found to be 11.6% in urban population of Chennai, Gupta HL, Yadav M et al<sup>19</sup> found the prevalence was 13.0% in Delhi Urban population, Similarly, according to Bai PV, Krishna Swamy CV et al<sup>16</sup> the prevalence was found to be 17.4% in Chennai Urban Population. This study has concordance with the Kutty VR et al<sup>17</sup> who observed a prevalence of 16.9% in Tiravananthapuram Urban Population. Wesk SK Munoz B et al<sup>21</sup> found to be 21.4% in the age group of 40 yrs and above. The above studies were conducted in different parts of the world and thus the considerable variations were found and may be considered as due to ethnic, genetic and life style and environmental changes.

On the other hand, impaired glucose tolerance (IGT) people are also increasing. In the present study the prevalence of IGT was 12.8%, which may be concordance with the several other studies – Ramachandran A, Snehalatha C et al<sup>20</sup> (2001) found the prevalence of IGT was 14 % among urban population of Chennai. Lee WR<sup>15</sup> (Singapore) et al found the prevalence of IGT was 15% and Iyer et al<sup>14</sup> found the prevalence was 8.6% in subjects below 50yrs and 13.4% in subjects older than 50yrs.

In the study population 14.5% prevalence of diabetes mellitus among males and 10.1% prevalence of diabetes mellitus among females. Some studies show a lower prevalence of diabetes mellitus among females. Misra A, Pandey RM et al conducted a study in Delhi and they opine that diabetes mellitus was recorded in 11.2% of males and 9.9% of females.

In the present study, about 24.6% of diabetics belonging to upper class, 15% were upper middle class, 7.8% were belonging to lower middle class, 11% were from upper lower class and lastly 4% belonging to lower class. This was divided into upper middle and upper class verses other socio economic class. The observed difference between these two and diabetes mellitus was statistically significant ( $P < 0.001$ ). High socioeconomic status significantly associated with Diabetes Mellitus.

Several other researchers found that socio economic status

is directly proportional to development of diabetes mellitus. Ramachandran A, Snehalatha C et al<sup>23</sup> Feb 2002 stated that diabetes mellitus is increased among high socio economic group. Same finding was observed by Ramachandran A, Snehalatha C et al<sup>20</sup> Sep 2002 in the same year conducted another study and found that prevalence of Diabetes Mellitus was more in high income group people group and was statistically significant ( $p=0.002$ )

In the study population, about 19.6% diabetics from sedentary activity, 9.1% were from moderate activity and only 6.9% diabetics from severe activity. Ramachandran A, Snehalatha C et al<sup>23</sup> (2002) conducted a study in urban population of Chennai and stated that physical activity is associated with the diabetes mellitus. Costacou T<sup>27</sup> (Columbia) et al reviewed that increased levels of physical activity would decrease the incidence of type 2 diabetes. According to Quinn<sup>22</sup> (Chicago) stated that physical activity inversely related with the type 2 diabetes mellitus.

In the study population 35.8% (270) were smokers and 64.2% (484) were non-smokers. Among the smokers, the Prevalence of Diabetes was 19.2% and non smokers the Prevalence of Diabetes was 7.0%. Several other researchers found the association of smoking with the diabetes. Similar finding was observed with the Montonen J, Knekt P et al carried out a study in Finland and found that smoking is not associated with the type 2 diabetes. Mas, Cutter J et al<sup>24</sup> conducted a study in Singapore and Kutty VR, Soman CR et al<sup>30</sup> conducted a study in Kerala and they found that the smoking has directly proportional to diabetes mellitus and the association was significant.

In the study population 27.1% (205) were consumed alcohol and 72.9% (499) were non-alcoholics. Among the Alcoholics, the Prevalence of Diabetes was 26.3% and non alcoholic persons the Prevalence of Diabetes was 6.4%. Among the Diabetics (Out of 86), 54 (62.7%) were consumed alcohol and 32 (37.3%) were non-alcoholic persons. MAS, Cutter J et al<sup>30</sup> (2003) and Ramachandran A, Snehalatha C et al<sup>20</sup> (2002) and they found the alcohol consumption significantly associated with diabetes mellitus. Lu W, Jablonski KA et al found that the alcohol consumption did not appear to significantly increase the risk for worsening glucose tolerance.

In the study population 230 (30.5%) were practicing exercise and about 524 (69.5%) were not practicing any kind of exercise. Among diabetics (86), 17 (19.7%) diabetics were practicing exercise and only remaining 69 (80.3%) were not practicing any exercise. Several other researchers found the same results. Naeem AG conducted study in Kashmir men and stated that exercise inversely related with diabetes mellitus. Ramachandran A, Snehalatha C et al<sup>20</sup> stated that diabetes mellitus indirectly related with the duration exercise.

Body mass index (BMI) is very important tool in the measurement of obesity. The above table shows about the Prevalence of Diabetes in the group of BMI <18.5 was 8.1%, BMI range between 18.5 to 25 was 9.0%, Prevalence of Diabetes was more in the BMI range of 25-30 was 18.5

and lastly diabetic Prevalence was in the BMI range of 30 plus was about 20.5%.

Where as in Diabetic population (Out of 86), less than 25 BMI range was about 50(58.1%) and BMI range above 25 was 36 (41.9%). Prevalence of type 2 diabetes mellitus associated with the high BMI (>25kg/m<sup>2</sup>) and statistically significant ( $\chi^2=58.18$ ,  $p<0.001$ ).

This study correlated with the Vikram NK, Misra AD et al conducted a study in New Delhi and defined that cut offs for defining obesity by BMI are lower than the suggested limit of 25 kg/m<sup>2</sup>, Kutty VR Soman AR et al<sup>30</sup> conducted a study in Trivandrum and observed high BMI (>25 kg/m<sup>2</sup>) associated with type 2 diabetes and also with the Misra A, Pandey RM et al<sup>70</sup> conducted a study in Delhi. In Ramachandran A, Snehalatha C et al<sup>22</sup> studies found the BMI associated with the type 2 diabetes, and Perry IJ conducted a study in Ireland and stated that BMI associated with the type 2 diabetes mellitus. Most of the studies revealed that BMI associated with type 2 diabetes.

Out of 86 diabetics, 30 (34.8%) people were giving father having Diabetes, about 16 (18.6%) were giving history of Mother having Diabetes and lastly 40 (46.5%) people were giving both parents having Diabetes Mellitus. This finding was correlated with De Silva SN, Weerasuriya N et al (2002) conducted a study in Sri Lanka, Oneyemere KV, and Lipton RB et al<sup>29</sup> conducted a study in Chicago and concluded that a positive parenteral history of DM appears to be more strongly related to childhood type 2 than type 1 Diabetes Mellitus. A similar finding was observed with the Ramachandran A, Snehalatha C et al<sup>20</sup> found that families with a positive family history of diabetes significantly associated with the type 2 diabetes mellitus.

Among diabetic males, 20 (58.8%) people were showing more than or equal to 94 cms waist circumference and 14 (41.2%) people were showing less than or equal to 94 cms waist circumference. Same finding was observed with the Yajnik CS conducted a study in Pune and Misra A, Pandey RM et al conducted a study in Delhi and stated that waist circumference directly related with diabetes mellitus.

Out of 86 Diabetic individuals, about 59 (68.6%) people were showing the dyslipidaemic condition and only less proportion of people 29 (33.4%) were showing normal eulipidaemic condition.

## Summary and conclusions

The Present study involves 754 urban slums population of Kadapa who were examined during one-year period from April 2009 to March 2010.

1. Of the 754 individuals screened, 86 were found to be suffering from type 2 diabetes mellitus, reflecting a prevalence of 11.4%.
2. The association between different age groups and diabetes mellitus was statistically significant and found that as the age advances the prevalence of diabetes also increasing.
3. A statistically significant association was observed between the high socio economic status and diabetes

mellitus ( $p<0.01$ ).

4. Physical activity associated with the type 2 diabetes mellitus.
5. There was significant association was found between Diabetes Mellitus with smoking and alcohol consumption
6. Body mass index was more in Diabetic individuals. BMI was strongly associated with the diabetes mellitus in the study population and the finding was statistically significant. ( $P<0.05$ )
7. Majority of Diabetics were giving the history of both parents suffered from Diabetes. Family history and Diabetes was statistically significant ( $P<0.01$ ).
8. More number of Diabetics having waist circumference of males (>94cm) and waist circumference of Females (>80cm) and this association was statistically significant.
9. Out of 86 diabetic individuals, about 68.6% people were showing dyslipidaemic condition and remaining people were normal.

Based on the above statistically significant associations, this warns the importance of life style modifications in the prevention of Type 2 Diabetes in the general public.

“DIABETES MELLITUS STILL REPRESENTS THE TIP OF THE ICEBERG”

## References

1. Zimmet P. Globalization, coca-colonization and the chronic disease epidemic, can the dooms day scenario be obverted, Jr. of Intern. Med. 2000; 247: 301 – 10.
2. King H, Aubert RE, Herman WH Global burden of Diabetes, 1995 – 2025, Prevalence, numerical estimates and projections Diabetes care: 1998; 21: 1414 – 31.
3. Ramachandran A Snehalatha C et al National Urban diabetes survey Diabetologia 2001; 44: 1999 – 101
4. Zargar Ah, Wani Al, Masooda MR, Laway BA, Basheer MI Mortality in Diabetes Mellitus, data from a developing region of the world. Diabetes Res. Clin. Pract. 1997; 43: 67 – 74.
5. B Jork S. The cost of diabetes and diabetes care Diabetes Res. Clin. Pract. 2001; 54 (suppl): 53 – 8.
6. Sanger TJ, Zimmet PZ Epidemiology of Type 2 diabetes An international perspective pharmaco economic 1995: 1 Suppl (8): 1-11.
7. Zimmet PZ Diabetes epidemiology as a tool to trigger diabetes research and care Diabetologic 1999: 42: 499 – 518.
8. Turtle JR The economic burden of insulin resistance Int. J. clin pract suppl 2000; 113: 23-8.
9. World Health Organization Diabetes Mellitus, Report of WHO Study group WHO Tech. Ref. Ser. No. 727, Geneva: WHO: 1985
10. Lanis MI, Zimmet P Classification of diabetes mellitus and other categories and glucose intolerance in: Alberts KGMM,
11. Report of the export committee on the diagnosis, and

- classification of diabetes mellitus. *Diabetes care* 2002; 25 (Suppl): S5 –20.
12. Report of the expert committee on the diagnosis and classification of diabetes mellitus. *Diabetes Care* 1997; 20: 1183 – 97.
  13. B.K.Mahazan *Methods in Biostatistics for medical students and research workers*, 6<sup>th</sup> edition, Published by Japee brothers, New Delhi, 1999; page no: 93.
  14. Iyer SR, Iyer RR et al Diabetes mellitus in Dombivli—an urban population study. *J Assoc Physicians India*. 2001 Jul; 49: 713-6.
  15. Lee WR (Singapore) The changing demography of diabetes mellitus in Singapore. *Diabetes Res Clin Pract*. 2000 Oct; 50 Suppl 2: S35-9.
  16. Bai PV, Krishnaswami CV et al Prevalence and incidence of type-2 diabetes and impaired glucose tolerance in a selected Indian urban population. *J Assoc Physicians India*. 1999 Nov; 47(11): 1060-4.
  17. Kutty VR, Soman Cr et al Random capillary blood sugar and coronary risk factors in a south Kerala Population. *J Cardiovasc Risk*. 2002 Dec; 9(6): 361-7.
  18. Ramachandran A, Snehalatha C et al Temporal changes in prevalence of type 2 diabetes and impaired glucose Tolerance in urban southern India. *Diabetes Res Clin Pract*. 2002 Oct; 58(1): 55-60
  19. Gupta HL, Yadav M et al A study of prevalence of health problems in asymptomatic elderly Individuals in Delhi. *J Assoc Physicians India*. 2002 Jun; 50: 792-5.
  20. Ramachandran A, Snehalatha C et al High prevalence of diabetes and impaired glucose tolerance in India: National Urban Diabetes Survey. *Diabetologia*. 2001 Sep; 44(9): 1094-101.
  21. Wesk SK, Munoz B et al Risk factors for type 2 diabetes and diabetic retinopathy in a Mexican – American Population *Am.J. Ophthalmology* 2002 Sep: 134 (3) : 390 – 8.
  22. Quinn L (Chicago) Behavior and biology: the prevention of type 2 diabetes. *J Cardiovasc Nurs* 2003 Jan-Mar; 18(1):62-8Related Articles, Links
  23. Ramachandran A, Snehalatha C et al Impact of poverty on the prevalence of diabetes and its complications in Urban southern India. *Diabetes Med*. 2002 Feb; 19(2): 130-5.
  24. Ma S, Cutter J et al Associations of diabetes mellitus and ethnicity with mortality in a multiethnic Asian population: data from the 1992 Singapore National Health Survey. *Am J Epidemiology*. 2003 Sep 15; 158(6): 543-52.
  25. Lu W, Jablonski KA, Resnick HE et al Alcohol intake and glycemia in American Indians: the strong heart study. *Metabolism* 2003 Feb;52(2):129-35Related Articles, Links.
  26. Misra A, Pandey RM et al High prevalence of diabetes, obesity and dyslipidaemia in urban slum Population in northern India. *Int J Obes Relat Metab Disord*. 2001 Nov; 25(11): 1722-9. *Int J Obes Relat Metab Disord*. 2002 Sep;26(9):1281.
  27. Mayer-Davis EJ, Costacou T (Columbia) et al Obesity and sedentary lifestyle: modifiable risk factors for prevention of type 2 diabetes. *Curr Diab Rep* 2001 Oct;1(2):170-6Related Articles, Links
  28. Ferreira SR, Lerario DD et al Obesity and central adiposity in Japanese immigrants: role of the Western dietary pattern. *J Epidemiol* 2002 Nov;12(6):431-8Related Articles, Links
  29. Onyemere KU, Lipton RB et al Parental history and early-onset type 2 diabetes in African Americans and Latinos in Chicago. *J Pediatr* 2002 Dec;141(6):825-9Related Articles, Links
  30. Kutty VR, Soman Cr et al Random capillary blood sugar and coronary risk factors in a south Kerala population. *J Cardiovasc Risk*. 2002 Dec; 9(6): 361-7.



# Cheiloscopy- a growing concept in forensic odontology

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## Introduction

The identification of the criminal or culprit and the victim in crime, accidents, mass disasters is of paramount importance from a social, emotional and legal view point. Lip prints have gained importance since there is a growing demand placed upon law enforcement to provide sufficient physical evidence to link a suspect to a crime or a contact between a victim and a suspect. Till date finger prints are considered to be the most important form of evidence but lip prints are gradually gaining importance in the forensic science arena.<sup>1</sup>

Any process that possesses the possibility of assisting the forensic field in identifying a suspect should be pursued and, if discovered pertinent, utilized in the act of criminal investigations and legal proceedings. The use of lip prints falls into this category and because they have been proved reliable and trustworthy to link a suspect to a crime, more emphasis should be given to this field.<sup>2</sup>

## Cheiloscopy

is a forensic investigation technique that deals with identification of humans based on lips traces.<sup>7</sup> Lip print analysis or

Cheiloscopy is a process that provides both qualitative and quantitative results thus its application in the forensic field should be widely accepted by both law enforcement and the legal professionals.

There is conclusive evidence that lip prints are suitable for the successful comparison, analysis and identification of a person to a crime. In fact there have been convictions of perpetrators who were positively identified via the analysis of their known lip prints to those found at the crime scene. Studies also indicate lip prints are classified as individual characteristics and similar to fingerprints, no two people possess the same prints.<sup>3</sup> Given this information, it is interesting to wonder whether lip prints are hereditary. The physical attributes regarding the shapes of family members' lips can clearly be identified as being hereditary.

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## Milestone studies

Lip prints have been with us since the beginning of man. Similar to the prints on a person's finger, lips also possess furrows that can be classified into various types for identification purposes. Unlike fingerprints however, lip prints have not been as popular a study due to limited

research in this field.

During the early 1900's, anthropologists merely mentioned the existence of lines on lips without providing any type of evidence or studies regarding their use in the forensic science field pertaining to identification. LeMoyné Snyder was the first one to introduce the possibility of utilizing lip prints to identify individuals. Hence he is considered the Father of cheiloscopy. In his studies, Snyder described an interesting case where in a woman was struck by a vehicle. During the investigation, a lip print was discovered on the left front fender of the vehicle suspected to have hit her. After comparing the lifted lip print to the female's lips, investigators discovered a match thus placing the vehicle at the scene of the crime.<sup>5</sup>

Perhaps the greatest research of Cheiloscopy completed has been from Japanese doctors Suzuki and Tsuchihashi in 1970 and 1974 wherein lip prints were obtained from 280 and 1,364 Japanese citizens (respectively).<sup>1</sup>

The research concluded "no lip print showed the same pattern in the investigation of 1,364 Japanese subjects (757 males and 607 females)." The study further stated: "With regard to the dissimilarity of the lip print, as far as the 1,364 subjects used in this study are concerned, there were no two identical lip prints."<sup>2</sup> This means that each human lip print has its own individual characteristics, and although the numbers so far studied are relatively small, it is noteworthy that the data indicate a strong possibility of the absolute dissimilarity of lip prints. Therefore, it may be concluded that the lip print can be used as one of the techniques for identification in the field of forensic odontology.

Dr. Suzuki examined 18 pairs of uni-ovular twins discovering numerous similarities between the lip prints but no exact match. He reported "It was assumed that personal lip prints may show dissimilarity amongst individuals, and that this lip groove pattern could be influenced by hereditary factors, some of which were formed by the study of twins. This finding was important information due to the fact both uni-ovular twins contain the same DNA but not the same fingerprints. The discovery of two different forms of physical identification for such twins was exciting and pertinent for the forensic science field."<sup>1</sup>

Other than the aforementioned collected lip prints from the twins, the only other analysis of lip prints connected with families was reported by Hirth, Gottsche and Goedde (1975). In this study, lip prints were obtained from 76

families for the purpose of determining whether there was a genetic basis of ridge-pattern in the lips. A branched pattern was prominent on the upper lips while simple patterns (long and short vertical grooves) were more frequent on the lower lips. The results of the study proved a genetic basis of lip prints.<sup>6</sup>

Lincoln C. Petersen conducted a study in 2006 to determine whether lip prints had hereditary characteristics or not. There were 81 participants comprising of 20 different biological families. From the research gathered in this study it was indicative that lip print characteristics are indeed hereditary, either directly from the parents or from the grandparents. It is also important to note that while the children possessed the same characteristics as their parents and/or grandparents, it should be stressed that the characteristics located on the lips were not in the exact location as their parents, suggesting each person possessed his/her own individually unique lip prints.<sup>6</sup>

Although limited research has been completed on the subject of Cheiloscropy and lip prints, a common response within all the literature reflects a positive indication for the utilization of lip prints for personal identification.

### Indian perspective

In India, research in the field of **Cheiloscropy** has been increasing. Not only have the laboratories developed a new technique in identifying suspects or criminals from the description of their lips, the Forensic Sciences Laboratory in Bangalore has established a comprehensive classification system for the micro-structural (grooves and wrinkles found on lips) and macro-structural (shape and size of lips) patterns of lips.

**Preeti Sharma, Susmita Saxena and Vanita Rathod** of the Department of Oral Pathology and Microbiology, Subharti Dental College, Meerut, UP conducted a study of lip prints in gender identification. They found that lip prints are useful in identification of gender as the lip pattern is different in males and females.<sup>7</sup>

**Murkey P.N., Sutay Seema, Khandekar I.L.** have studied lip print pattern, the relationship of gender, and genetic composition with lip print in 204 individuals of Sewagram of Maharashtra including 10 groups of twins. They found that persons with similar genetic composition had similar lip prints but there was no exact match.<sup>7</sup>

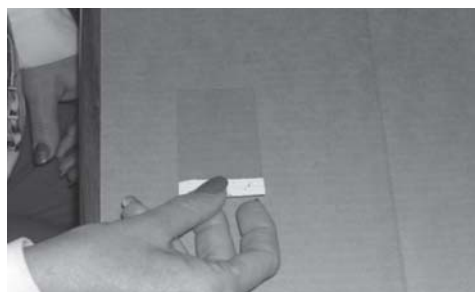
**Dr. Anil Aggarwal**, Professor of Forensic Medicine has studied in detail the importance and uniqueness of lip prints. The author suggests that lip prints are a unique feature and can be used as an adjunct to finger prints.<sup>7</sup>

### Techniques

There are two methods of recording Lip prints. In the first method, the person simply presses his or her lips onto a piece of plastic that is subsequently processed with black magnetic detection powder. While the latent print is successful in being developed, the characteristics are

somewhat difficult to analyze utilizing a common, household magnifying glass. It would stand to reason that these prints would be greatly enhanced using more advanced technological instruments found in a forensic laboratory. The first method of obtaining lip prints is by utilizing a cut piece of clear plastic on which the lip print would be placed. Using a black magnetic detection powder, the latent lip prints are then developed. This method serves as a twofold experiment. The first being a positive way to develop a latent lip prints such as the way one would be discovered at an actual crime scene. The second positive result is the the fact that the latent lip prints can be successfully developed after five months. As with any experiment, this procedure is accomplished by adhering to extremely specific directions.<sup>8</sup>

#### Photograph 1:



The second method in obtaining lip prints is the use of lipstick and blank index cards. Two lip prints are obtained on one index card for two reasons; the first is the possibility that one print may contain clearer lines over the other. Secondly, it goes to reason that the applied lipstick may be extremely heavy (depending on how forceful the participant is). By rolling the lips on the card the second time using the same applied lipstick, some may be clearer

#### Photograph 2:



#### Photograph 2:



as the first sample removed the thicker layer of lipstick. The same thought process applies when lifting a latent print at a crime scene that was developed with powder. The first lift is often dirty in appearance due to excessive powder while the second lift obtains a cleaner looking print. The process is extremely helpful in analyzing, as two prints are available on one card.<sup>8</sup>

## Types of lip prints

Type I represents a lip possessing full vertical grooves.

Type I! (pronounced "one-dash") has partial grooves running vertically on the lip.

Type II represents branched grooves.

Type III represents intersected (diamond) grooves that look similar to crosses.

Type IV represents the reticular (rectangular) pattern similar to wire mesh or boxes .

Type I (Full Vertical Grooves)



Type II (Short Vertical Grooves)



Type II (Branched Grooves)



Type III (Diamond Grooves)



Type IV (Rectangular Grooves)



Because most lips contain more than one type of pattern, the lips are divided into four quadrants. Each quadrant is studied and the various types of lip prints are recorded. Each quadrant is read from the center of the lip outward toward the corner of the lip. The upper and lower lips are divided through the center by an imaginary vertical line, thus producing left and right upper and lower quadrants. A branched pattern is prominent on the upper lips while simple patterns (long and short vertical grooves) are more frequent on the lower lips.<sup>7</sup>

## Conclusion

Lip prints are hereditary yet considered to be individualistic, each possessing their own unique characteristics. For this reason it is safe to suggest lip prints can and should be included in the forensic sciences arena as a legitimate means of identifying persons of interest connected with criminal activity.

Of course lip prints may never be on the same level as fingerprints when it comes to identification; however, it is interesting to know that certain countries around the world are creating databases and programs centered around the characteristics and appearances of lips specifically for the purpose of solving crimes.

## References

1. Suzuki, K., Tsuchihashi, Y. Personal Identification by Means of Lip Prints. *Journal of Forensic Medicine*, 1970; 5: 52 – 57.
2. Tsuchihashi, Y. Studies on Personal Identification by Means of Lip Prints. *Forensic Science Journal*, 1974; 15: 233 – 248.
3. Castello, A., Alvarez, M. & Verdu, F. Just Lip Prints? *The FASEB Journal*, 2004; (7): 615 – 616.
4. Ehara, Y. & Marumo, Y.. Identification of Lipstick Smears by Fluorescence Gas Chromatography. *Forensic Science International*, 2004; (10) : 1 – 10.
5. Hansen, M. The Fine Print. *ABA Journal*, 2000 ;(18): 134-138.
6. Hirth, L., Gottsche, H. & Goedde, H.W. Lip Prints— Variability and Genetics, *National Library of Medicine*, 1975; (15): 47 – 62.
7. Kasprzak, J. Cheiloscopy. *Forensic Science International*, 2000; (5) : 358 – 362.
8. Kasprzak, J. Possibility of Cheiloscopy. *Forensic Science International*, 2002; (7) : 145 – 151.

# Safety and efficacy of PGE2 gel (cerviprime) for induction of labour in term prelabour rupture of membranes, with special reference to its fetomaternal complications

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## Abstract

This study evaluated the safety and efficacy of PGE2 gel in 100 patients for induction of labour in term PROM and compared it with control of 100 patients. Mean duration of latent phase, mean total duration of labour and mean admission-delivery interval, rate of Caesarian section, Incidence of fetal and neonatal morbidity was statistically decreased as compared with control.

## Keywords

PGE2 gel (cerviprime), term prom, fetomaternal complications.

## Introduction

Passage through birth canal is the shortest but probably the most hazardous journey made by any individual in his or her life. Modern obstetrics aims at culmination of every pregnancy in a healthy baby and healthy mother. Prevention is the foundation stone of successful obstetrics. Modern obstetrics requires to foresee the problems of labour and to anticipate them and then to construct a plan of action at proper time. So that masterly inactivity is replaced by masterly activity. In majority of pregnant women rupture of fetal membranes occur with or after the onset of labour pains.

The standard definition of premature rupture of fetal membranes, which has been accepted by American College of Obstetrician and Gynecologists, is rupture of fetal membranes prior to the onset of labour, regardless of gestation age. When rupture of membranes occur at or > 37 completed weeks of gestation but before onset of labour, it is *Term Prelabour Rupture of Membranes*.

It is important to confirm the diagnosis of PROM and gestation age, as incorrect diagnosis can subject the patient to the iatrogenic risk of preterm delivery, tocolysis and corticosteroid administration and cesarean section. On the other hand delayed diagnosis and delay in the initiation of treatment leads to fetomaternal morbidity and mortality. Maternal complications with delayed intervention are intrapartum infections, chorioamnionitis,

endometritis, dry labour, dysfunctional labour, increased incidence of operative and instrumental deliveries, cord prolapse, abruptio placentae, PPH, persistent occipitoposterior position, septicemia and shock. Fetal complications include preterm delivery, fetal pulmonary hypoplasia, fetal limb defects, sudden IUD due to cord prolapse or abruptio placentae, sepsis, increased neonatal morbidity due to dysfunctional labour, operative and instrumental delivery, neonatal sepsis, respiratory distress syndrome etc. So due to above mentioned risks, for management of Term PROM, masterly activity i.e. induction of labour is preferred over masterly inactivity i.e. expectant management

## Material and methods

This case control study comprised of 100 patients of term pregnancy with spontaneous prelabour rupture of membranes taken as cases (group I) and 100 patients of term pregnancy with spontaneous prelabour rupture of membranes who were managed conservatively, were taken as control group (group II). The intervention had been done in cases by inducing them with intracervical PGE2 gel (Cerviprime) which is available as prefilled syringes.

Data was collected from the cases admitted in labour room at Panna Dhai Govt. Mahila Chikitsalaya associated with RNT medical college, Udaipur, between December 2004 to December 2005.

Inclusion criteria are, only primigravidae and second gravidae, PROM at term (>37 weeks), singleton pregnancy, cephalic presentation, no uterine activity, absent membranes and cervical dilatation <3 cm. Exclusion criteria are acute sepsis, patient in active labour with cervical dilatation > 3 cm, APH, cord prolapse, PROM > 12 hrs., contracted pelvis, fetal distress and meconium stained liquor, allergic to prostaglandins.

Detailed history including basic demographic data along with complete obstetric history was taken. Diagnosis of PROM had been confirmed by sterile speculum examination to demonstrate the presence of amniotic fluid in posterior fornix and positive ferning and absence of membranes on per vaginal examination. After confirming the Gestation age, proper counseling is done and written informed consent had been taken. Bishop's score was calculated in every patient in both the groups. Injectable antibiotics had been administered in all patients in both

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the groups. In group I induction was done with intracervical PGE2 gel, and in group 2 Expectant management was followed.

### Observations and discussions

Table no-1 shows the incidence of PROM in present study was 3.2% and the incidence of PROM at term was 2.5%. Similar findings have been found by other authors. Sanyal et al (1990) study shows incidence of PROM at term 2.6%, Klebanoff et al (1995) 5-15%, Fernando (2003) 2.7-17%.

Table no- 2 show mean age of patients in group I is 23.93+/-

- 3.05 years and group II, 24.31+/-3.91 years. Maximum patients (63%) were in the age group of 21-25 years. Similar findings have been reported by other authors in their study Akhtar et al (1980) 21-30 yrs, Nirmala Panday et al (2001) 21-25 yrs.

Table no-3 shows maximum patients (90%) of group I and 93% from group 2 belong to middle and low socioeconomic status. Similar findings have been reported by other authors in their study; Rao et al (1993) 90.1%, Anjana Devi et al (1996) 88.4%, Nirmala Panday et al (2001) 86%. In the study maximum patients, 60% of group I and 55% of group II were primigravidae. No significant differences were found in the two groups regarding age,

**Table 1:** Incidence of PROM in Present Study

S.N.	Particulars	No.	% age
1	Total no. of deliveries at Panna Dhai Mahila Chikitsalaya from Dec.04 to Dec.05)	13,289	
2	Total no. of cases of PROM	426	3.2%
3	Total no. of cases of PROM at term	328	2.5%

**Table 2:** Distribution in relation to Maternal Age

S.N.	Age(Years)	Group I		Group II	
		N=100	%	N=100	%
1	16-20	13	13%	14	14%
2	21-25	62	62%	63	63%
3	26-30	23	23%	15	15%
4	31-35	02	02%	05	05%
5	36-40	-	-	03	03%
Mean Age(Years)		23.93+/-3.05		24.31+/-3.91	

**Table 3:** Distribution of patients in relation to basic socio-demographic factors

	Group I		Group II	
	N=100	%	N=100	%
Registration				
Registered	83	83%	82	82%
Unregistered	17	17%	18	18%
Residing area				
Urban	74	74%	78	78%
Rural	26	26%	22	22%
Socio-Economic Status				
High	07	07%	10	10%
Middle	52	52%	50	50%
Low	41	41%	40	40%
Parity				
0	55	55%	60	60%
1	45	45%	40	40%

**Table 4:** Distribution in Relation to Bishop's Score at Admission

S.N.	Bishop's Score at Admission	Group I		Group II	
		N=100	%	N=100	%
1	0-3	54	56%	30	30%
2	4-7	46	46%	69	69%
3	8-11	-	-	01	01%
Mean Bishop's Score		3.4+/-1.5		4.2+/-1.3	

(P< 0.001)

parity, socioeconomic status, antenatal registration and duration of rupture of membranes at admission as may be seen in table no-3.

Table no-4 shows, in the present study, mean bishop's score in group I was 3.4+/-1.5 and group II was 4.2+/-1.3. This difference was found significant with (p <0.001). Thakur et al (1995) reported Bishop's score < 6 in his study on PROM. Mean duration of rupture of membranes at admission in group I was 4.73+/-3.56 hrs and group II was 4.35+/-3.67 hrs. This difference was statistically not significant.

Table no-5 shows distribution of patients in both the groups in relation to duration of latent phase. Mean duration of latent phase in group I was 4.63+/-1.57 hrs and in group II was 6.57+/-1.96 hrs. The difference was found to be statistically significant, (p<0.001). Table no-6 shows distribution of vaginally delivered patients in the two groups in relation to total duration of labour. Mean total duration of labour in group I was 7.98+/-2.44 hrs and in group II was 10.37+/-2.11 hrs. This difference was found statistically highly significant (p<0.001). Similar study was

done by Zamzami et al in 2005 and found that mean duration of labour was significantly lower in PROM group, induced with intracervical PGE2 gel.

Table no-7 shows distribution of patients delivered vaginally in relation to admission delivery interval in the two groups. Mean admission-delivery interval in group I was 9.03+/-2.17 hrs and in group II was 11.98+/-2.35 hrs. The difference was significant statistically, (p <0.001). Similar findings were reported by Hidar S et al (2000) admission delivery interval was 19.5+/-6.2 hrs in his study.

Table no-8 shows the distribution of patients in the two groups in relation to mode of delivery. In the present study, 96% of group I patients had normal delivery and in group II, 86% had normal delivery and 4% were delivered by forceps. In group I cesarean delivery rate was 4% and in group II 10%. Maternal morbidity due to operative and instrumental delivery was found to be higher in control group. Similar findings have been reported by other authors, in PROM managed expectantly, Meikle SF (1992) reported cesarean delivery rate 10%, Lettau R(1995) 15.5%.

**Table 5:** Distribution of patients in the two groups in relation to Duration of latent phase

S.N.	Duration of Latent Phase (Hrs.)	Group I		Group II	
		N=100	%	N=100	%
1	0-3	16	16%	7	7%
2	>3-6	64	64%	27	27%
3	>6-9	20	20%	66	66%
Mean Duration of Latent Phase (Hrs)		4.63+/-1.57Hrs.		6.57+/-1.96Hrs	

(P <0.001)

**Table 6:** Distribution of vaginally delivered patients in the two groups in relation to Total Duration of Labour

S.N.	Total Duration of Labour(Hrs.)	Group I		Group II	
		N=96	%	N=86	%
1	0-5	22	22.9%	02	2.3%
2	>5-10	60	62.5%	34	39.6%
3	>10-15	14	14.6%	50	58.1%
Mean Duration of Labour (Hrs.)		7.98+/-2.44 Hrs.		10.37+/-2.11 Hrs.	

P <0.001

**Table 7:** Admission Delivery Interval in the Patients delivered vaginally in the two groups.

S.N.	A-D Interval(Hours)	Group I		Group II	
		N=96	%	N=86	%
1	0-5	06	6.3%	02	2.32%
2	>5-10	59	61.5%	28	32.55%
3	>10-15	29	30.2%	56	65.11%
4	>15-20	02	02%	0	0%
Mean A-D Interval		9.03+/-2.17 hours		11.98+/-2.35 hours	

(P <0.001)

**Table 8:** Distribution of Patients In Relation to Mode of Delivery

S.N.	Mode of Delivery	Group I		Group II	
		N=100	%	N=100	%
1	Normal Delivery	96	96%	86	86%
2	Forceps	0	0%	04	04%
3	Cesarean Section	04	04%	10	10%

**Table 9:** Distribution of Cases according to cause of LSCS in the two Groups

S.N.	Indications of LSCS	Group I		Group II	
		N=04	%	N=10	%
1	Fetal Distress	1	25%	4	40%
2	Non Progress of Labour	3	75%	6	60%
3	Failed Induction	0	0%	0	0%

**Table 10:** Neonatal Complications

S.N.	Neonatal Complications	Group I		Group II	
		N=100	%	N=100	%
1	Meconium Staining	1	1%	4	4%
2	Asphyxia	1	1%	6	6%
3	RDS	-	-	-	-
4	Septicemia	-	-	2	2%
5	Jaundice	-	-	-	-
6	Aspiration Pneumonia	-	-	-	-
7	ICH	-	-	-	-
8	Diarrhoea	-	-	-	-
9	NN Mortality	-	-	-	-
10	No Complications	98	98%	88	88%

P < 0.001

**Table 11:** Maternal Complications

S.N.	Maternal Complications	Group I		Group II	
		N=100	%	N=100	%
1	Prolonged Labour	0	0%	6	6%
2	PPH	0	0%	1	1%
3	Cervical Tear	2	2%	0	0%
4	Gaped Episiotomy	0	0%	0	0%
5	Chorioamnionitis	0	0%	0	0%
6	Pyrexia	0	0%	1	1%
7	Maternal Mortality	0	0%	0	0%
8	No Complications	98	98%	92	92%

Bilgin (2003) reported in his study, in PROM induced with PGE2 gel, cesarean section rate 5% and Zamzami TY (2005) reported 4.5%.

As may be seen in Table no-9, the distribution of patients according to the causes of cesarean section. *Fetal distress* was the cause of cesarean section in 40% of patients of group II who had undergone cesarean section (n=10) and in 25% (n=1) of group I patients who had undergone cesarean section (n=4).

Mortality Table no-10 shows the relation of neonatal complications in the two groups. In group I, 1% of the neonates had asphyxia and, 1% had meconium staining. 98% of neonates in group I had no complication. In group II, 4% of neonates had meconium staining, 6% had asphyxia and 2% had septicemia and 88% had no complications. Incidence of *neonatal morbidity* in group I was 2% and in group II was 12%. This difference was statistically significant (p < 0.001). So there is a direct correlation of PROM with neonatal outcome. The rate of neonatal sepsis increases with PROM as concluded in the study of Lettau et al 4% in 1995 and Akyol et al (1999).

Table no-11 shows the relation of maternal complications with the two groups. It can be seen from the table that in

group I 2% patients had cervical tear and 98% patients had no complications. In group II, 6% patients had prolonged labour, 1% had PPH and 1% had pyrexia and 92% had no complications. As previously seen in table no-8, maternal morbidity, due to instrumental and operative delivery, is also higher in group II (control). Mielke et al (1992) had reported chorioamnionitis 6.8% and endometritis 2% in his study on term PROM. Anjana et al (1996) had reported chorioamnionitis 5.76% and PPH 1.9% in her study on Term PROM induced with intracervical PGE2 gel.

## Conclusion

Our present study concludes that intracervical PGE2 gel can be safely used as a method of induction of labour in Term PROM without any significant maternal and fetal complications. This method can reduce the rate of cesarean section in Term PROM.

## References

1. Akhtar M.S., Deacon I.A., Wren F. (1980). J of Obstet & Gynaecol India 30:81.
2. Akyol D. Mungan T, Unsal A. (1999) Aust NZ J Obstet

- Gynaecol 1999 Aug.; 39(3) : 291-5.
3. Anjana Devi. Complication of PROM : Chorioamnionitis, PPH, Puerperal Infections. J of Obstet and Gynaecol, India 1996; 46:63.
  4. Atlay R.D., Sutherest JR. (1970) Am. J. Obstet & Gynaecol 108 : 993.
  5. Averette HE, Hopman B.C., Fergusson (1963) Am. J Obstet & Gynaecol 87 : 226.
  6. Bada MDS, Henxetta. Asphyxia Neonatorum. Thepedeart Clin North Am 1977; 24: 3-91.
  7. Ben Haroush A, Kalpan B, Bar J (2004) Am J of Obstet and Gynaecol. 2004 July21(5) 263-8.
  8. Benedetto C, Tibaldi C, Sozzani P, (2004) J Maternofetal Neonatal Med 2004 Nov; 16 Suppl. 2:9-12.
  9. Bernstein P, Leland N, Gurland P, Yare D (1987) Am J Obstet and Gynaecol 156:336-40.
  10. Bilgin T, Kadioglu M. (2003) J Mater Fatal Neonatal Med. 2003 Sep. 14(3) : 158-62.
  11. Bishop E.H. (1964) Obset & Gynaecol 24 : 226-268.
  12. Brosen I. Gordon H. (1965) Br. J. of Obstet and Gynaecol 72:342.
  13. Deborah A, Ray MD, Thomas J, Yarite MD (1992) Am J Obstet and Gynaecol 166:836-43.
  14. Goeschen K. (1989) Am. J. Perinatol (1989) Apr: 6(2) : 181-4.
  15. Goes K. Premature Rupture of Foetal Membrances at Term : Indication of Labour with Endocervical Prostaglandin E<sub>2</sub> Gel or Intravenous Oxytocin Am J Perinatol 1989 Apr; 6(2) : 181-4.
  16. Gonen R, Samberg I, Degani S. Intracervical Prostaglandin E<sub>2</sub> for induction of labour in patients with premature rapture of membranes and an unripe cervix. Am. J Perinatol. 1994 Nov;11(6):436-8.
  17. Granstorm L., Ekman G, Ulinstan U; Acta Obstet. Gynecol Scand. 1987;66(5): 429-31.
  18. Hidar S, Bibi M, Jerbi M, Bouguizene S, Khairi H. (2000) J. Gynaecol Obstet. Biol Reprod. (Paris) 2000 Oct.; 29(6) : 607-13.
  19. Kiilholma P, Gronroos M. (1984) Obstet and Gynaecol Invest 17 : 194 (Quoted From McGregor,1996)
  20. Klebanoff MA, Regan J.A. (1995) Am. J. Obstet & Gynaecol 172;658
  21. Kovavisarach E., Sermask P. (2000) Aust NZ J. Obstet Gynaecol, 2000 Feb; 40(1) : 30-2
  22. Lettau R, Hege G, Steldinger R. Premature rupture of foetal membranes at term: an indication for induced labour with prostaglandis? Zentralbl Gynkol. 1995; 117(3) : 121-5
  23. Lettau R., Hege G., Steldinger R, Zentralbl Gynkol (1995); 117(3) : 121-5
  24. Malik N, Gittens L, Gonzzalez D, Bardeguez A, Ganesh V, Apuzzio Clinical amnionitis and endomentritis in patients with premature rupture of membranes: endocervical prostaglandin E<sub>2</sub> gel versus oxytocin for induction of labour. J. Obstet Gynaecol. 1996 Oct;88 (4 Pt 1):540-3
  25. Miekle SF, Biselle ME: Freedman (1992). Obstet & Gynaecol 1992 July; 80(1) : 76-9
  26. Milasinovic L, Redeka G. (1997) : Med. Pregi. 1997 May-June; 50(5-6) : 175-80
  27. Nirmala Pandey (2001) Obstet & Gynaecol TODAY (2003) Vol. VIII(9) 24-27.
  28. Sanyal M.K. (1990) Indian J of Obstet & Gynaecol 40;623.
  29. Thakur U, Maitra N, Baxi S, Hazra N (1995) Indian J Matern Child Health 1995 Jan-Mar 6(1); 14-6.
  30. Zamzami TY (2005) Arch Gynaecol Obstet 2005 Oct. 6; 1-5.



# Acute neurotoxicity with appropriate dose of Isoniazid: A case report

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## Abstract

### Report

Isoniazid (INH) is most frequently used in combination with other drugs for the treatment of tuberculosis or as monotherapy for treatment of latent tuberculous infection. Seizures due to anti-tubercular chemotherapy are a rare side effect. INH causing status epilepticus has been very rarely reported to cause seizures. We present a patient who, after 5 months of treatment with appropriate dose of INH, evolved to status epilepticus. Seizures could be controlled only after administering of pyridoxine.

### Keywords

Isoniazid, Acute neurotoxicity, Status epilepticus, Seizures, Pyridoxine.

### Introduction

There have been several reports of INH causing seizures<sup>1-2</sup> and this effect is thought to be due to the inhibition of GABA synthesis in the CNS. Review of all the cases of drug-induced seizures reported to the California Poison Control System revealed that of 386 cases, 23 (5.9%) was due to INH<sup>3</sup>. It is among the most common causes of drug-induced seizures in United States<sup>4</sup>. Therapeutic doses of INH may occasionally precipitate convulsions in patients with known epilepsy or in patients with subclinical deficiency of pyridoxine that is seen in pregnancy, cancer, uraemia or chronic liver disease<sup>5</sup>.

### Case history

A 26-year-old male was started on category-I antituberculosis treatment under RNTCP, which contains INH 600 mg/alternate day about 5 months ago, after being found to be smear positive. He developed seizures at home after his dinner and was brought to our hospital via 108 emergency ambulance services. He received 10 mg of diazepam intravenously in the ER (emergency room) that stopped his seizure for 2-3 minutes. His seizure started again and

he received, in ER, 4 mg of lorazepam and 600mg of phenytoin intravenously without any control over seizures. He was started on phenytoin drip. Seizuring activity could not be controlled for the next 2 hours. Considering the history of consuming INH, we gave him 2gm of pyridoxine (50 tablets of 40 mg each crushed and administered through ryles tube as injection pyridoxine was not available). The seizures disappeared after 90 minutes. Other possible causes of seizures were meticulously ruled out. His sodium was 140 Meq/L, potassium 4.0 Meq/L, and chloride 112 Meq/L. The blood sugar level was 140mg/dL. The serum calcium, magnesium and phosphate level were within normal limits. Liver function test (LFT), amylase, lipase and ammonia level were within normal limits. HIV was nonreactive. CT scan of brain did not reveal any obvious pathology, like a mass or hemorrhage that could lead to seizures. After regaining consciousness the patient informed that he was taking only recommended dose of INH alternate day. He also denied any history of epilepsy. INH was restarted after 3 days. After second dose of INH patient again developed status epilepticus which was controlled using same dose of pyridoxine and other anticonvulsants. Later on INH was omitted from the regimen. 6 months of follow up by the patient remained uneventful without any seizure.

### Discussion

Side-effects to anti-tubercular drugs are fairly common but there are a few side effects that are rare. INH is one of the most effective and cheapest among anti-tuberculous drugs. It is rarely associated with serious adverse effects that include hepatitis, peripheral neuropathy, cutaneous reactions and mental changes<sup>6</sup>. Ingestion of toxic amounts of INH causes recurrent seizures, profound metabolic acidosis, coma and even death. In adults, toxicity can occur with the acute ingestion of as little as 1.5 g of INH. Doses larger than 30 mg per kg often produce seizures<sup>7</sup>. However, our patient denied any history of overdose. To present with severe acute INH neurotoxicity, in the absence of overdose or any comorbid condition that would predispose to such a severe adverse reaction is rare. Review of literature reveals that, there have been less than ten cases of routine dose of INH causing seizures reported earlier. Symptoms of neurotoxicity are most likely due to an inhibition of vitamin B6 metabolism and thereby depletion of gamma-aminobutyric acid (GABA) in the CNS so the administration of pyridoxine, an antidote for INH-induced seizures<sup>8-10</sup>.

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Treatment of INH toxicity must address correction of  $\alpha$ -aminobutyric acid deficiency with pyridoxine replacement and management of life-threatening events. For poisonings in which the amount of INH ingested is known, pyridoxine is dosed on a gram-for-gram basis<sup>11</sup>. In the management of the comatose patient as well as those with status epilepticus, it is recommended that intermittent infusions of pyridoxine 5 g/5 min mixed with 5% to 10% dextrose and water be administered. This infusion can be repeated every 20 minutes<sup>12</sup>. In severe toxic reactions, exchange transfusion<sup>13</sup>, peritoneal dialysis<sup>14</sup>, and hemodialysis<sup>15</sup> have been efficacious in removing this drug from the bloodstream because protein and tissue binding is minimal.

## Conclusion

Pyridoxine deficiency should be suspected and its supplementation initiated in any patient on antituberculous treatment presenting with seizures and metabolic acidosis even if there is no history of overdose. Prognosis is good when treatment is administered early.

## References

1. Temmerman, W, Dhondt A, Vandewoude K. Acute isoniazid intoxication: seizures, acidosis and coma. *Acta Clin Belg.* 1999; 54: 211–216
2. Asnis DS, Bhat JG, Melchert AF. Isoniazid overdose: four case reports and review of the literature. *Ann. Pharmacother.* 1993; 27:444–446
3. Thundiyil JG, Kearney TE, Olson KR. Evolving epidemiology of drug-induced seizures reported to a Poison Control Center System. *J Med Toxicol.* 2007;3(1):15-9.
4. Bloch AB, Rieder HL, Kelly GD, Cauthen GM, Hayden CH, Snider DE. The epidemiology of TB in the U.S.: implications for diagnosis and treatment. *Clin Chest Med.* 1989;10:297-313.
5. Alvarez FG, Guntupalli KK. Isoniazid overdose: four case reports and review of the literature. *Intensive Care Med.* 1995;2:641-4.
6. Girling DJ. Adverse effects of anti-tuberculosis drugs. *Drugs.* 1982;23:56-74
7. Romero JA, Kuczler FJ. Isoniazid overdose: recognition and management. *Am Fam Physician.* 1998;57(4):749-52.
8. Wallace, K. L. Antibiotic-induced convulsions. *Crit. Care Clin.* 1997;13:741–762
9. Williams, H. L. and Bain, J. A.: Convulsive effect of hydrazines: relationship to pyridoxine. *Int. Rev. Neurobiol.* 1961;3: 319–348
10. Wason S, Lacouture P. G, and Lovejoy F. H. Single high-dose pyridoxine treatment for isoniazid overdose. *JAMA.* 1981;246:1102–1104
11. Minns, Alicia B, Ghafouri, Nazli, Clark, Richard F. Isoniazid-Induced Status Epilepticus in a Pediatric Patient After Inadequate Pyridoxine Therapy. *Pediatric Emergency Care.* 2010; 26:380-81
12. Lheureux, Philippe; Penalosa, Andrea; Gris, Mireille. Pyridoxine in clinical toxicology: a review. *European Journal of Emergency Medicine.* 2005;12(2):78-85
13. Katz BE, Carver MW. Acute poisoning with isoniazid treated by exchange transfusion. *Pediatrics.* 1956;18:72-6.
14. Cocco AE, Pazouek LJ. Acute isoniazid intoxication management by peritoneal dialysis. *N Engl J Med.* 1963;269:852-3.
15. Konigshausen TH, Altrogge G, Hein D, Grapensee B, Potter J. Hemodialysis and hemoperfusion in treatment of most severe INH poisoning. *Vet Hum Toxicol.* 1979;21:12-15.

# Soft drinks and oral health- A review

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## Abstract

Soft drink consumption has increased dramatically across all demographic groups, especially among children and teenagers. Soft drinks have many potential health problems, including dental caries and enamel erosion. Soft drinks containing inherent acids and sugars have both acidogenic and cariogenic potential. Many studies showed a positive relationship between caries and dental erosion and the consumption of soft drinks. Compared with caries, dental erosion seems to have much stronger relationship with soft drinks. It is necessary to educate patients about the harmful effects of excessive soft drink consumption and to advise them with the following tips to prevent dental erosion and caries: limiting soft drinks intake, choosing the low erosive soft drinks, improving the drinking habit, avoiding brushing tooth within 1 hour after consuming acidic food, and using fluoride toothpaste.

## Keywords

Soft drinks, dental caries, erosion

## Introduction

Urbanization and economic development result in rapid changes in diet and lifestyles. Market globalization has a significant and worldwide impact on dietary excess leading to chronic diseases<sup>1</sup>. In socioeconomically developing countries, the change from a traditional lifestyle to a Western lifestyle has, among other things, led to an increase in sugar consumption from food and beverages<sup>2</sup>. Soft drink consumption has increased dramatically across all demographic groups, especially among children and teenagers. The popularity of soft drinks has been increasing year after year, due in part to their sweet taste, and in part to the aggressive and pervasive advertising campaigns run by soda companies<sup>3</sup>.

## Soft drink

Soft drink (also referred to as soda, pop, soda pop or fizzy drink) is a non-alcoholic beverage typically containing water and a flavoring agent. Many are carbonated and sweetened, and may contain additional ingredients such as fruit juice.

## Composition

The first carbonated soft drinks, which were named as such

in order to clearly differentiate them from hard, alcoholic beverages, and the technology to make them, were imported from the Europeans, who had discovered how to force carbon dioxide gas into water back in the sixteenth century. The original bubbly drinks were carbonated mineral waters mimicking those found in therapeutic natural springs and the first of these were patented in the United States in 1810<sup>4</sup>. Generally compositions of soft drink are:

**Sugar:** Most of the soft drinks contain the monosaccharide glucose and fructose and the disaccharide sucrose<sup>5</sup>.

**Artificial Sweetener:** like aspartame, acesulfame-K, saccharin or sucralose. These sweeteners have a number of possible side effects: migraines, memory loss, heart complications, depression and increased cancer risk.

**Caffeine:** Caffeine is used to increase the flavor in soft drinks, but it is also very addictive. Caffeine stimulates the nervous system and increases the heart rate. It also increases slightly the excretion of calcium.<sup>6</sup>

**Carbon Dioxide:** Carbon dioxide makes soft drinks fizz but it is also a waste product.

**Phosphoric or Citric Acid:** Acids are added to soft drinks to give them a nice tingling feeling when they are swallowed. These acids also act as a preservative to keep the soft drink fresh and crisp-tasting.

**Preservatives:** Preservatives are put into soft drinks so that they last longer. However, Juicing-for-health.com explains that preservatives like sodium benzoate or sulfur dioxide can cause asthma, rashes, hyperactivity, fainting, shock, or a coma.

**Coloring:** Soft drinks may contain artificial coloring. These coloring ingredients make the drink look more appealing to drink. For example, caramel coloring agent gives the drinks a rich brown color. Artificial colorings, especially Yellow No. 5, promote attention-deficit hyperactivity disorder in some children. Yellow No. 5 also causes hives, asthma, and other allergic reactions in a small number of individual.<sup>6</sup>

## Impact on health

Excessive consumption of soft drinks adversely affects health. While there are questions regarding artificially sweetened diet soft drinks and their effect on health, the evidence that consuming soft drinks sweetened with sugar or high fructose corn syrup can result in harmful effects

has been thoroughly researched and documented.<sup>7</sup>

In 1998, the Center for Science in the Public Interest published a report which examined statistics relating to the soaring consumption of soft drinks, particularly by children, and the consequent health ramifications, including tooth decay, nutritional depletion, obesity, osteoporosis, type-2 diabetes, and heart disease.<sup>6</sup>

## A danger to oral health

Soft drinks contain high amounts of sugar and acids, which are added to give sodas their characteristic good taste. Unfortunately, both these components pose significant risks to oral health. Soft drinks have many potential health problems, including dental caries and enamel erosion.

## Dental caries

Dental caries may result from a long-term high intake of soft drinks. When sucrose intake exceed 15-20 kilograms per person per year is directly associated with caries prevalence, when sucrose is consumed between meals. 375 ml can of soft drink contain in excess of 40 gm of sucrose, thus one can of sugared soft drink per day for 1 year will in itself account for 15 kilograms of sucrose per year.<sup>8</sup>

A frequent exposure to dietary acids will have ecological effects on the oral biofilm and can shift the supra gingival oral flora toward aciduric micro-organism. As the intra-oral pH falls, the number and proportion of aciduric organism such as mutans streptococci and lactobacilli increases, and the proportions of acid – sensitive species fall. The reduction in pH caused by the drink not only enhances the competitiveness of cariogenic organism, but also inhibits the growth and metabolism of non –caries associated species.<sup>8</sup>

A recent large study of young children in Iowa found “intake of regular soda pop was the strongest predictor of the extent of caries”<sup>6</sup>. There is also a strong association between the frequency of between-meal consumption of soda pop and caries.<sup>9,10</sup>

Strong associations between high DMFS (decayed missing filled surfaces on teeth) scores and soft drink consumption in persons aged 25 and above have been seen. Serious problems will occur particularly in people who have dry mouths (caffeine, medications, exercise and certain ailments cause dry mouth).<sup>11</sup>

It has also been observed that the children with a high carbonated soft drink consumption pattern showed significantly higher caries experience, even compared with those children with a high juice consumption pattern<sup>12</sup>. The reason being sugar substrates in 100% juice are primarily fructose and glucose, whereas the substrate in regular soda pop and regular beverages from powder is sucrose and/or high-fructose corn syrup (i.e., fructose and glucose). Glucosyltransferase from *Streptococcus mutans* uses sucrose but not fructose or glucose to form extracellular glycans that facilitate dental plaque

adherence to the enamel surface. Linkages between glycans are rigid and increase the porosity of the plaque, which could facilitate diffusion of sugars and acid within the plaque and increase caries risk. In the laboratory, sucrose seems to promote *Streptococcus mutans* selection<sup>10</sup>.

## Dental erosion

Dental erosion (erosive tooth wear) is the situation of a chronic loss of dental hard tissue that is chemically etched away from the tooth surface by acid and/or chelation without bacterial involvement. Soft drinks containing inherent acids and sugars have both acidogenic and cariogenic potential.<sup>13</sup> Many studies showed a positive relationship between caries and dental erosion and the consumption of soft drinks.<sup>14,15</sup> Compared with caries, dental erosion seems to have much stronger relationship with soft drinks.<sup>13</sup>

It is found that over time, exposing dental enamel to carbonated beverages weakens and permanently destroys enamel.<sup>16,17</sup>

Regular black soft drink contains orthophosphoric acid. It is well known that orthophosphoric acid will dissolve the protective pellicle layer deposited by saliva onto teeth, and will etch both enamel and dentine. Citric acid in soft drink sequesters calcium ions from saliva, preventing remineralization, etches dentine and causes dental erosion.

More importantly, these various acids are effective buffers, giving the drink high titratable acidity and making their pH reducing effects in the mouth greater than the protective buffering action of saliva. This explains why enamel and dentine hardness decreases after exposure to soft drinks and erosion areas develop.<sup>8</sup>

In an study carried out by researchers at the University of Melbourne, showed damage to tooth enamel by acid erosion was reported by 25-45% of those surveyed.<sup>18</sup> Sugared versions of soft drinks proved to be more erosive than their diet counterparts.<sup>19</sup>

The erosive potential of drinks is mainly represented by their pH and the buffering capacity. Carbonated drink could reduce surface hardness of enamel and dentine. Carbonated drinks have lower pH than fruit juices. The buffering capacities are in the following order: fruit juices > fruit-based carbonated drinks > non-fruit-based carbonated drinks.<sup>13</sup>

Studies have shown that dental erosion is also associated with the drinking methods. Holding the drink longer in the mouth leads to a more pronounced pH drop<sup>14</sup>. Drinking with an increasing flow rate and with decreasing outlet diameter could increase the erosion depth. The effect is also strengthened when acid temperature grows higher.<sup>13</sup>

## Prevention

**Individual approach:** Obviously, lowering or eliminating soft drink consumption entirely is not a very likely solution.

1. Substitute different drinks with beverages containing less sugar and acid such as water, milk and 100 percent fruit juice.<sup>20</sup>
2. Rinse with water: After consuming a soft drink, flush your mouth with water to remove vestiges of the drink that can prolong exposure of tooth enamel to acids.<sup>16</sup>
3. Avoid any erosion-inducing habits such as sipping, swishing or holding drinks in the mouth. Do not brush teeth for at least one hour after an erosive challenge (such as consumption of a highly acidic beverage).<sup>21</sup>
4. Fluoride toothpaste and mouth rinse: Fluoride reduces cavities and strengthens tooth enamel, so brush with a fluoride-containing toothpaste s. Rinsing with a fluoride mouthwash also can help.
5. Professionally applied fluoride treatment.<sup>22</sup>

**For school children:** American Dental Association opposes contractual arrangements in schools that promote increased access to soft drinks for children, thereby influencing consumption patterns.<sup>4</sup>

The American Academy of Pediatrics has stated that the “providing soft drinks in schools can lead to childhood obesity” and should focus on providing more nutritious, lower calorie beverages such as water, milk, 100% fruit juice and vegetable juice. Communities and schools are uniting across America to pass legislation banning the sale of soft drinks in schools especially during meal times. However, much more effort needs to focus on competitive foods, foods sold at school stores and at fundraisers.<sup>1</sup>

**Public Health approach:** The Center for Science in the Public Interest offers the following suggestions for reducing the consumption of soft drinks.<sup>6</sup>

- Individuals and families should consider how much soda pop they are drinking and reduce consumption accordingly. Parents should stock their homes with healthful foods and beverages that family members enjoy and, for the most part, not keep soft drinks—especially non-diet drinks—in the refrigerator.
- Physicians, nurses, dentists, and nutritionists should routinely ask their patients how much soda pop (and other low-nutrition foods) they are consuming and advise them, when appropriate, to consume less.
- Labels on non-diet soft drinks should state that frequent consumption of those drinks promotes obesity, diabetes, and tooth decay, osteoporosis and other health problems.
- Local, state, and federal governments should be as aggressive in providing water fountains in schools, government buildings, parks, and other public spaces as the industry is in placing vending machines.
- School systems and other organizations catering to children should stop selling or advertising soft drinks.
- Organizations concerned about children’s health, dental and bone health, heart disease, and cancer should collaborate on campaigns to reduce soft drink consumption.
- State and local governments should consider levying small taxes on soft drinks.

- Federal agencies should sponsor more scientific research to further explore the effects of soft drink (and refined-sugars) consumption on nutrient intake, obesity, dental caries and erosion, osteoporosis, kidney stones, and heart disease.

## Perspective from soft drink industry trade association

Soft drink consumption has become a highly visible and controversial public health and public policy issue. The industry trade association in the United States (the American Beverage Association, formerly the National Soft Drink Association) counters nutrition concerns with several key points: (1) the science linking soft drink consumption to negative health outcomes is flawed or insufficient, (2) soft drinks are a good source of hydration, (3) soft drink sales in schools help education by providing needed funding, (4) physical activity is more important than food intake, and (5) it is unfair to “pick on” soft drinks because there are many causes of obesity and there are no “good” or “bad” foods. Similar positions have been taken by other trade associations such as the British Soft Drinks Association and the Australian Beverages Council.<sup>23</sup>

## Conclusion

The contemporary changes in beverage patterns have the potential to affect oral health. Though there is limited epidemiological evidence assessing the association between oral health and soft drink consumption, it consistently indicates that soft drinks adversely affect dental caries and enamel erosion. Although the diseases are different in their histological appearance, the two conditions occurring concurrently could be deleterious to dental hard tissues. Moreover, numerous in vitro and animal studies have consistently shown enamel erosion with the use of soft drinks. Given this evidence it would seem appropriate to encourage children and adolescents to limit their intake of soda.

## Reference

1. WHO: Risks to oral health and intervention: Diet & nutrition- WHO [www.who.int]
2. Anne Nordrehaug Åstrøm, Joyce Rose Masalu: Oral health behavior patterns among Tanzanian university students: a repeat cross-sectional survey: BMC Oral Health. 2001;1(1):2.
3. Joseph Devine: Soft Drinks - A Danger To Your Oral Health: EzineArticles.com
4. American Dental Association - Diet and Oral Health – Oral Health Topics-ADA; www.ada.org
5. Martin-Villa MC, Vidal-Valverde C, Rojas-Hidalgo E: Soluble sugars in soft drinks: Am J Clin Nutr. 1981 Oct; 34(10):2151-3.
6. Michael F Jacobson, Liquid Candy: How Soft Drinks are Harming Americans’ Health: Centre for Science in the Public Interest, Washington DC 1998; 2nd Ed. 2005: 1-

- 28.
7. Erin O'Brien: Harmful Effects of Drinking Soft Drinks: May 2010: eHow.com
  8. Walsh, Laurence J: Black cola drinks, oral health and general health: an evidence-based approach: Oral health issues. ADA News Bulletin, 372 December: 22-24.
  9. Al Ismail, BA Burt, and SA Eklund: The cariogenicity of soft drinks in the United States: J Am Dent Assoc, Vol 109, No 2, 241-245
  10. Teresa A. Marshall, Steven M. Lev, Barbara Broffitt, John J. Warren, Julie M. Eichenberger-Gilmore, Trudy L. Burns, Phyllis J. Stumbo, P: Dental Caries and Beverage Consumption in Young Children: Pediatrics Vol. 112 No. 3 September 2003, pp. 184-191.
  11. Australian Dental Association: The Truth About Black Cola Drinks And Dental Health: National Dental Update: ADA: November 2008-www.ada.org.au
  12. W. Sohn, B.A. Burt, M.R. Sowers: Carbonated Soft Drinks and Dental Caries in the Primary Dentition: Journal of Dental Research: March 2006 vol. 85 no. 3 Pg- 262-266
  13. Ran Cheng, Hui Yang, Mei-ying Shao, Tao HU, Xue-dong: Dental erosion and severe tooth decay related to soft drinks: a case report and literature review: Journal of Zhejiang University science B; 2009 10(5):395-399
  14. Ann-Katrin Johansson, Peter Lingström, Thomas Imfeld, Downen Birkhed: Influence of drinking method on tooth-surface pH in relation to dental erosion: European Journal of Oral Sciences: Volume 112, Issue 6, pages 484-489, December 2004
  15. Luo Y, Zeng XJ, Du MQ, Bedi R: The prevalence of dental erosion in preschool children in China. J Dent. 2005 Feb;33(2):115-21.
  16. Soda Attack: Soft Drinks, Especially Non-colas and Iced Tea, Hurt Hard Enamel: Oral Health Resources: General Dentistry July/August 2004 issue- www.agd.org.
  17. J. Anthony von Fraunhofer, Matthew M. Rogers: Dissolution of dental enamel in soft drinks: General Dentistry July/August 2004 issue:308-12
  18. Australian dental association: Drinks and Dental Decay: ADA: Aug 2005- www.ada.org.au
  19. Jain P, Nihill P, Sobkowski J, Agustin MZ: Commercial soft drinks: pH and in vitro dissolution of enamel: Gen Dent. 2007 Mar-Apr;55(2):150-4; 155, 167-8
  20. Colgate world of care: Soda or Pop? It's Teeth Trouble by Any Name: Oral & Dental Health Basics - www.colgate.com
  21. Aubrie Mazza: Oral hygiene habits of college students: unhealthy eating and high levels of stress put them at risk: Health Care Industry-Access, Jan, 2008
  22. Brimacombe C: The effect of extensive consumption of soda pop on the permanent dentition: A case report. Northwest Dentistry 2001;80:23-25.
  23. Lenny R. Vartanian, Marlene B. Schwartz and Kelly D. Brownell: Effects of Soft Drink Consumption on Nutrition and Health: A Systematic Review and Meta-Analysis: April 2007, Vol 97, No. 4 American Journal of Public Health 667-675.

# Health economics-economic evaluation in dental public health

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## Abstract

Economic evaluation provides a method of systematically comparing the costs and outcomes of alternative health care programmes. It is now used increasingly to provide planning information. Economic evaluation is necessary to produce the best health care and maximum benefit with minimum cost to the community based on available resources. Health economics is a branch of Economics concerned with issues related to scarcity in the allocation of health and health care. A key concept of health economics is the opportunity cost of a programme, which can be described as the value of the resource when it is put to its best alternative use. Therefore, health economics is about resource management – what is affordable and desirable and what is not. As the health of the population will not be improved just by spending more money on health care, the understanding of health economics is essential to properly implement the economic policies for the health care enhancements. Hence, the policy makers and the dental personnel should have adequate knowledge regarding the same for providing better health services.

## Keywords

health economics, cost analysis, health policies

## Introduction

“We never will have all we need. Expectation will always exceed capacity... This service must always be changing, growing and improving; it must always appear inadequate.”<sup>1</sup>

Health economics is defined as an assessment of the most effective use of available resources, defined in terms of costs and outcome. Despite the improvement in health seen in the majority of countries, cost of health care have continued to rise above the general rate of inflation. This is due to a number of factors, such as the price of materials, personnel wages and the use of more advanced technology. Health will not be improved by just spending more money on health care. On the other hand new technological developments have led the ability to provide more treatment that may be more expensive. Health economics is therefore, about resource management what is affordable and desirable and what is not. When resources are scarce, decisions need to be made as to how best to allocate them.<sup>2</sup>

Evaluation of health care programs depends on evaluation of availability, effectiveness, efficiency and efficacy. The evaluation of efficiency is more commonly known as economic evaluation. Thus, economic evaluation may be defined as “the comparative analysis of alternative courses of action in terms of both their costs and consequences.”<sup>1</sup>

## Why is economic evaluation important?

India is the second most highly populated country of the world and has changing socio-political-demographic and morbidity patterns that have been drawing global attention in recent years. Despite several growth-orientated policies adopted by the government, the widening economic, regional and gender disparities are posing challenges for the health sector.<sup>3</sup>

First, with increasing life expectancy the epidemiological transition points towards greater incidence of non-communicable or lifestyle diseases. This goes hand in hand with a continuing serious problem of communicable and preventable diseases. Second, there is a lot of variation in the public provisioning of health care - a state subject. Poor states are hard pressed for funds. Third, India is an exception across countries in that nearly four-fifths of its health care expenditure is out-of pocket. Health expenditure by Indian Government is only 0.8% of the total GDP. Thus, health care resources are limited by the total funds available. Coupled with the burgeoning growth of unregulated private sector care-givers, this has serious implications. These three issues open up a number of policy questions on access to, utilisation, economic evaluation and quality of health care.<sup>3</sup>

It has been proposed that, faced with increased demands, but little increase in resources, the National Government in Health Sector can work:-

- 1) To become more efficient so that more individuals can be treated with the same resources.
- 2) To extend means testing so that some people may be excluded from certain services due to their wealth.
- 3) To increase ‘rationing’ or to provide a smaller range of services.

Hence, the aim is to maximize health from available resources while paying due concern to issues of equity. Allocation of funds is generally on two levels: planning and clinical. For planning decisions, this involves deciding whether or not facilities should be provided at all and, if so, where they should be located. Clinical decisions are

then made by practitioners on behalf of individual patients or group of patients. A programme that looks attractive from a patient's viewpoint may look decidedly unattractive from the government's budget. The use of beta-interferon in the treatment of multiple sclerosis is a good example of this. It was found that benefits of interferon beta-1b were very low relative to its cost and estimated that in order to treat sufficient patients to prevent one individual becoming wheelchair bound would cost over 1 million pounds.<sup>1</sup>

### **What does economic evaluation involve?**

It deals with costs and benefits. The basics of economic evaluation involve identifying, measuring, valuing and comparing the costs and benefits of alternatives being considered. Robinson classified costs as:

Direct costs-health services costs, other related services, costs incurred by patients and families. These are generally primary costs of the health care programme. Health service costs include staff costs and consumables, capital costs, overheads. Patient costs include out of pocket expenses, labour costs for caregivers, patient lost earnings.<sup>4</sup>

Indirect costs include loss of productivity and costs borne by society. They are secondary costs that relate to paid and unpaid productive work.<sup>4</sup>

Cost may also be subdivided into those borne by the health agencies both govt. and private (staff, hotel services, drugs), those borne by the patient and family (for example, travel), and cost to the rest of the society (for example, health education).<sup>1</sup>

The benefits of an intervention are usually health improvements, which can be measured in a number of ways including:

- 1) Health effects, for example, cases found, cases prevented, lives saved.
- 2) Economic benefits that can be measured in direct (savings in health care cost because the program make the person healthier), indirect (individuals are able to return to work), and intangible benefits (monetary value of the reduction in pain and suffering).
- 3) Value of health improvement itself by the patient, family and society regardless of the consequences

The real cost of health care intervention is the opportunity cost-what is the loss of the health outcomes if an intervention is forfeited. The aim of economic evaluation is to ensure the benefits of a programme is greater than the opportunity cost of the programme.<sup>4</sup>

### **Methods of economic evaluation**

The basic tasks of any economic evaluation are to identify, measure, value and compare all costs and consequences. Although the theoretical price of a resource is its opportunity cost, the pragmatic approach to costing is to use existing market prices. The widespread use of charges (the amount paid

to the provider by a third party payer) instead of the identification of real costs is a typical example, since it is not certain that these charges reflect actual costs. Costs arise from the use of resources within the health sector, resources used by patients and families and resources used in other sectors.<sup>4</sup>

**Drummond et al<sup>5</sup>, Donaldson<sup>6</sup>, Robinson<sup>7,8,9,10</sup> and Kumar et al.** assessed the various methods available to evaluate economics of health care and to place in context how these methods may be used within dentistry. Four standard methods exist for full economic evaluation.<sup>4</sup>

#### **1) Cost –minimization analysis**

It is used to compare two interventions that have same expected outcomes. The costs are assessed and least costly is identified. This method is limited as few procedures/interventions will have the same outcomes.

#### **2) Cost effectiveness analysis**

It is used when outcomes vary but are expressed as common units. Costs are measured and effectiveness is defined in appropriate units, e.g. per life saved. It cannot be used where units of outcome vary, e.g. a treatment for reduction in caries had different outcomes to treatment for oral cancer.

#### **3) Cost –utility analysis**

It is a step further where outcomes are expressed as utility measures. These are cardinal values assigned to health states and are a measure that an individual holds for certain states of health or disease. Frequently, this is expressed as QALY (Quality Adjusted Life Year). This analysis is common when comparing two interventions for a disease.

#### **4) Cost –benefit analysis**

It is considered to be a more flexible method. It places monetary values on treatment costs (inputs) and consequences (outcomes). The results can be expressed in terms of a ratio of costs to benefit or the net benefit (loss) due to the treatment. It is an absolute cost of treatment. Cost-benefit and cost-utility analysis both address the issue of outcome valuation and, therefore, shed more light on whether certain treatments are worthwhile. In contrast, cost-minimization and cost-effectiveness assume that the intervention is worthwhile. However it is important to realize that none of these analyses can be used to replace sensible judgements, but may be used as an adjunct to decision-making.<sup>1</sup>

### **Economic evaluation in dentistry**

Consumers in health care market are now well aware about what services they need to buy and which providers offer the best value proposition. It is likely that there will be an increased demand for economic analyses of dental intervention by the public and by those funding health care. Private insurance companies are likely to demand increased evidence of value for money in the future. This is particularly important in fields that may be perceived as



'cosmetic'.

To date, the analysis that have been used most frequently are cost-effectiveness and cost-benefit and studies have focused largely on comparison of restorative materials<sup>11</sup> and preventive techniques.<sup>12</sup> **Bouckoms et al** in 1987 evaluated the cost effectiveness of alternative methods (non-surgical & surgical procedures as well as the use of antimicrobial agents) periodontal disease control. Data on costs were obtained from ADA publications of average charges for periodontal services. The concept of quality-adjusted tooth-years (QATYs) was developed to provide an outcome measure. Results showed that conservative non-surgical treatments not only have costs lower than surgical alternatives, but also maximize expected QATYs and antimicrobial therapy used as an adjunct to non-surgical treatment is likely to be both clinically effective and cost-effective.<sup>13</sup>

One of the good examples of cost benefit evaluation in dentistry is Dental Tourism. Patients may travel abroad for affordable dental care for treatment which is generally expensive in their own country. If there are extensive waiting lists, patients are more likely to travel to a country where they get top quality care at a low cost. India is emerging as one of the preferred destinations for dental tourism in the world.<sup>4</sup>

**Fox et al** in 2000 used a utility approach in which they developed a questionnaire using the aesthetic component of the Index of Treatment Need and found that patients seeking orthodontic treatment gave lower utility values for the aesthetic components 5 and 8 than those not wanting treatment.<sup>14</sup>

There are relatively few cost-utility studies in the field of dentistry, which probably reflects the increased difficulty and time-consuming nature of such studies. However, these are more useful because treatments frequently produce improvements in quality of life. In addition, QALY-based investigations in dentistry would also allow comparison of dental interventions with other forms of medicine.<sup>1</sup>

## Economic evaluation in preventive dentistry

The dental diseases and problems that pose the greatest burden to most communities are dental caries, periodontal problems, oral cancer and trauma. These can be largely prevented through a combination of community, professional and individual strategies. Economic evaluation has been done in the fields of Pit and fissure sealants, School based fluoride varnish programs, School based fluoride mouth rinsing programs, Community water fluoridation and Oral health promotion program.

**Pit and fissure sealants:** Various studies have been conducted to economically evaluate the application of pit and fissure sealants which states that fissure sealants are cost effective as it costs 4 to 6 times more to treat a tooth than to seal.<sup>15</sup>

Application of sealants by dental auxiliary staff further adds

to its cost effectiveness.<sup>16</sup>

**Morgan MV, Crowley SJ and Wright C** conducted a study on "Economic evaluation of a pit and fissure sealant and fluoride mouth rinsing program in two nonfluoridated regions of Victoria, Australia" in 1998. The study proved that the incremental cost-effectiveness ratio comparing intervention to control group varied between a net saving of \$7.00 to a cost of \$35.60 per DMFS avoided.<sup>17</sup>

Community water fluoridation

Various studies have been conducted to economically evaluate the C/B ratio for water fluoridation. It has been estimated to be 1:50 that is for every dollar spent on community fluoridation, the resultant saving will be \$50.<sup>18</sup>

**S P Klein, H M Bohannon, RM Bell and et al** conducted a study on "The cost and effectiveness of various types and combinations of school-based preventive dental care. It was found that community water fluoridation was the most cost-effective means of reducing tooth decay in children compared to combined effects of dental health lessons, brushing and flossing, fluoride tablets and mouth rinsing and professionally applied topical fluorides.<sup>19</sup>

## School based fluoride varnish or fluoride mouth rinsing program

**Ulla Moberg Sk Old, Lars G. Petersson, Downen Birkhed et al** conducted a study on "cost analysis of school-based fluoride varnish and fluoride rinsing programs" in 2008. Results showed that the outcome of fluoride varnish treatment in reducing approximal caries was better and the cost was lesser.<sup>20</sup>

**Yoshihara A, Kobayashi S, Yagi M and et al** conducted a study to evaluate the benefits of a school based fluoride mouth rinsing in a community dental health program. It was found that the cost-benefit ratio obtained through the caries reduction in 16 years is 18.8 and the cost-effectiveness ratio was 137 yen.<sup>21</sup>

Dental Health Education Program

C/B and C/E of a long-term DHE program (3 yrs for infants aged 8 months and mothers) for the prevention of ECC through home visits was evaluated. Comparisons were made with a slow releasing fluoride device (SRFD), community water fluoridation (CMF) & school based fissure sealant program (FSP). The cavities saved over the three year period indicated a B/C ratio for the DHE of 5.21 compared with SRFD of 4.17; CWF of 1.15 & FSP of 0.42. The C/E results were 1.92, 2.40, 8.66 & 23.74 respectively.

A study was conducted to examine whether oral-health promotion programs provided as an occupational health service for employees were cost-beneficial for employers. The subjects were composed of 357 male workers (20-59yr of age) who participated in oral-health promotion programs conducted at their workplaces between 1992 and 1997. The design of this study was a quasi-experimental study design in which the three programs (light: 1 visit; medium: 2-4 visits; and heavy: 5-6 visits) were compared through cost-benefit analysis conducted from

the viewpoint of the employers. The programs consisted of oral-health checkups by dentists and oral-health education, including that on the proper brushing method, by dental hygienists. The benefit/cost ratios of the three programs were 2.45, 1.46, and 0.73, respectively. These results suggest that a worksite oral-health promotion program of medium frequency is cost-beneficial for employers.<sup>22</sup>

## Conclusion

Economic evaluation is an accepted method for the appraisal of health care programs. Although it is used widely in medicine, its use in the field of dentistry is likely to become increasingly important in the future. The clinicians and policy makers need to understand the basics of these techniques if they are to play a part in the decision-making process. The application of the principles of economic evaluation is necessary to design health services that produce the best health care for the community based on available resources.

## References

1. Susan J.Cunningham. An introduction to economic evaluation of health care. *Journal of Orthodontics* 2001;28(3):246-250
2. Blanaid Daly, Richard Watt, Paul Batchelor and Elizabeth Treasure. *Essential dental public health*. Oxford University Press 2002; Edition 1:317-318
3. Srijit Mishra. *Public Health Scenario in India*. Indira Gandhi Institute of Development Research 2008.
4. Brenda Gannon. Economic Evaluation of dental treatment benefit scheme. *European Journal of Orthodontics* 2002;28:1-13
5. Drummond, M. F., Stoddart, G. L. and Torrance, G. W. (1987) *Methods for the Economic Evaluation of Health Care Programmes*, Oxford University Press
6. Donaldson, C. The state of the art of costing health care for economic evaluation 1990. *Community Health Studies*; 14: 341–356
7. Robinson, R. Costs and cost-minimisation analysis. *British Medical Journal* 1993; 307: 726–728.
8. Robinson, R. Cost-effectiveness analysis, *British Medical Journal* 1993; 307: 793–795.
9. Robinson, R. Cost-utility analysis, *British Medical Journal* 1993; 307: 859–862.
10. Robinson, R. (1993e) Cost-benefit analysis, *British Medical Journal* 1993; 307: 924–926
11. Mjor, I.A. Long term cost of restorative therapy using different materials. *Scandinavian Journal of Dental Research* 1992; 100: 60–65
12. Klock, B. Economic aspects of a caries preventive program. *Community Dentistry and Oral Epidemiology* 1980; 8: 97–102
13. Bouckoms. Cost effectiveness analysis of periodontal disease control. *Journal of Dental Research* 1987; 66: 1630–5.
14. Fox, D., Kay, E. J. and O'Brien, K. D. A new method of measuring how much anterior tooth alignment means to adolescents 2000. *European Journal of Orthodontics*; 22: 299–305.
15. SS Hiremath. *Textbook of Preventive and Community Dentistry*. Elsevier publishers 2007; Edition 1: 408–409
16. Margaret M. Walsh. The Economic Contribution of Dental Hygienists' Activities to Dental Practice. *Journal of Public Health Dentistry* 2007; 47(4): 193–197
17. Morgan, M.V., Crowley, S.J. and Wright, C. Economic evaluation of pit and fissure dental sealant and fluoride mouth rinsing program in two nonfluoridated regions of Victoria, Australia. *Journal of Public Health Dentistry* 1998; 58: 19–27
18. James R Mellberg, Louis W. Ripa and Gary S. Leske. *Fluorides in Preventive Dentistry*. Quintessence publishing Corporation.
- 19) S P Klein, H M Bohannan, R M Bell, J A Disney, C B Foch and R C Graves. The cost and effectiveness of school based preventive dental care. *Journal of Public Health Dentistry* 1997; 43: 18–25
20. Ulla Moberg Sk Old, Lars G. Petersson, Downen Birkhed and Anders Norlund. Cost analysis of school –based fluoride varnish and fluoride rinsing programs. *Acta Odontologica Scandinavica* 2008; 66(6): 286–292
21. Yoshihara A, Kobayashi S, Yagi M and Horii K. Benefits of a community oriented fluoride mouth rinsing program. *Nippon Koshu Eisei Zasshi* 1993; 40(11): 1054–61
22. Ichihashi Toru, Muto Takashi and Shibuya Koji. Cost-Benefit Analysis of a Worksite Oral-Health Promotion Program. *Ind Health* 2007; 45(1): 32–36.

# Public-private partnership: A revolution in antenatal health management

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## Abstract

Maternal mortality remains one of the most daunting public health problems in resource-poor settings, and reduction in maternal mortality has been identified as a prominent component of Millennium Development Goals (MDG 5)<sup>1,2</sup>. The productivity of public health sector in meeting these goals has been rather low, and it is often considered one of the 'sick unit'. Public-Private Partnership seems to be a 'treatment' to this 'sickness'<sup>3</sup>. It can play a significant role in determining whether success or failure is achieved in working towards goals for safe motherhood in many low- and middle-income settings. Though established private providers, especially nurses/midwives, have the potential to contribute to safe motherhood practices if they are involved in the care continuum, it is a subject of considerable debate that can or should private organizations provide public healthcare services? What is the scope for private finance in public healthcare services? Therefore this paper reviews some of the arguments for and against public or private ownership management and financing of public healthcare services in the field of antenatal care. It concentrates on health services, where non-economic values and ethical questions are as important as the efficiency considerations, and on health purchasing or funding organizations<sup>4</sup>.

## Keywords

Maternal Mortality Public-Private Partnership Antenatal Care Emergency Obstetric Clinic (EmOC) Millennium Development Goals (MDG 5)

## Introduction

Developing countries are currently struggling to achieve the Millennium Development Goal Five of reducing maternal mortality by three quarters between 1990 and 2015. Many health systems are facing acute shortages of health workers needed to provide improved prenatal care, skilled birth attendance and emergency obstetric services – interventions crucial to reducing maternal death. Complicating matters further, health workforces are typically concentrated in large cities, while maternal mortality is generally higher in rural areas. Each year, roughly 27 million women give birth in India<sup>4</sup>. Of these, about 136 000 die as a direct result of their pregnancy and delivery<sup>5</sup>. India accounts for more than 20% of the global burden of maternal mortality and the largest

number of maternal deaths for any country<sup>6</sup>. Most of these deaths are caused by haemorrhage (29%), anaemia (19%), sepsis (16%), obstructed labour (10%), unsafe abortion (9%) and hypertensive disorders of pregnancy (8%)<sup>7</sup>. This situation is particularly tragic because no new technologies or drugs are needed to radically lessen maternal mortality. Evidence has shown that access to and utilization of high-quality Emergency Obstetric Care (EmOC) is central to efforts aimed at reducing maternal mortality. Besides, community-based and hospital maternity care services, would lead to dramatic reductions in these unacceptably high ratios.

## Factors leading to maternal mortality

In developing countries, a woman's lifetime risk of dying from pregnancy and related complications is almost 40 times greater than that of her counterparts in developed countries.

In many under-resourced areas, particularly at the district health system level, there is a dearth of skilled care providers practicing within the public health system. In many of these areas, private sector facilities and practitioners that provide comprehensive essential obstetric care exist, often providing higher-quality services than public sector services, but the poorest women often cannot afford the fees, and thus cannot access these services.

In rural areas where majority of Indians still live, it is often difficult to access Emergency Obstetric Care (EmOC) facilities in case of need. Then, the barriers such as distance, transport cost, problems with supplies of medicines at the district hospital and poor staff attitudes towards the poor remain. Due to these barriers, many women hesitate to travel and seek care at a far away place and die at home or in transit if they decide to travel<sup>2</sup>. Studies conducted in Indian states of Andhra Pradesh, Maharashtra, and Rajasthan found that 42% to 52% of maternal deaths occurred at home or in transit to a hospital. A major part of the remaining causes for maternal mortality owes it to the deliveries conducted by the untrained local "Dais".

The social norms and a range of cultural factors influence the decision on childbirth and childcare practices. For example, in rural areas home delivery is preferred to institutional deliveries and pregnancy is looked upon as a condition that does not require medical attention. Decision to seek medical advice during delivery is delayed by the family and these result in maternal mortality. Most of these

deaths in India could be prevented by timely intervention in proper healthcare facility.

Today, strategies are more appropriately focused. It is essential that pregnant women in whom complications develop have access to the medical interventions of emergency obstetric care (EmOC) to ensure favorable maternal and fetal outcomes. Programmes to make such care more widely available include upgrading the infrastructure of community health centers and referral hospitals, and providing necessary and essential drugs, supplies and equipment for the timely delivery of services at all hours. In addition, staff with the appropriate obstetric training and skills in sufficient numbers should be deployed to facilities that offer maternity services. The referral systems between communities and health facilities also need to be strengthened.

### Potentials of private sector in health care

The private sector is an important source of care for poor and disadvantaged groups within low- and middle-income countries. For instance, in Guatemala, 40 to 45% of the population in the two lower income quintiles sought care in the private sector and in South Africa over 33% of each of the three lower quintiles did so<sup>10</sup>. Similarly, in Nepal, the private sector provided care to more than a third of the lowest income quartile<sup>11</sup>. A review of Demographic Health Survey (DHS) data from 38 countries found high levels of private sector use by those in the lowest socioeconomic quintile. In seeking to extend coverage of priority interventions, there are numerous operational advantages to working with pre-existing, self-sustaining outlets that are widely used by target populations. For these reasons the private sector represents an important potential partner in efforts to scale up coverage of effective health interventions among the poor<sup>12</sup>.

### Private sector interventions

A preliminary review identified eight areas of intervention involving the government or NGOs working with the private for-profit sector:

**1. Social marketing** is the application of the tools and concepts of commercial marketing to social and health problems<sup>13</sup>, in order to increase population coverage of effective and affordable interventions<sup>14</sup>. Social marketing interventions may include a combination of promotional activities, branding, labeling, pre-packaging, and subsidy of public health products. Application of social marketing increased condom use among women in urban Cameroon from 58% to 76%<sup>15</sup>, coverage of iron-folic acid supplementation from 6% to 99% in non-pregnant Filipino women<sup>16</sup>, and insecticide treated nets (ITN) coverage in rural Tanzanian children under 2 years from 10% to 61%<sup>17</sup>.

**2. A voucher** is a form of demand-side subsidy that the recipient can use as part or full-payment for a product or service from identified providers. The distribution of vouchers can be targeted, to improve access for an

identified population group such as the poorest households or pregnant women. Vouchers can either be competitively redeemed where they are exchangeable at a number of different providers<sup>14</sup>, or non-competitive where they are assigned to one particular provider<sup>18</sup>. The voucher intervention has been implemented in Chiranjeevi Yojana in Gujrat. Besides, the Kilombero and Ulunga Insecticide-Treated Net project (KINET) in Tanzania distributed vouchers reducing the price of nets at retail shops by 17% were distributed to pregnant women and mothers of under-five children attending public clinics<sup>19-21</sup>.

**3. Pre-packaging** is a strategy to improve provider and patient adherence to treatment regimens, and involves packaging drugs in pre-defined doses adequate for the targeted population group and length of treatment regimen<sup>22</sup>. Two interventions combined social marketing with prepackaged treatments – for Sexually Transmitted Infection treatment for male urethritis in Uganda<sup>23</sup> and prepackaged treatment for childhood malaria and acute respiratory infections in Nigeria<sup>24</sup>.

**4. A franchise** is a contractual arrangement between a health service provider and a franchise organization. It aims to improve access to quality- and price-controlled services. Providers are monitored by the franchise organization, which in public health is generally a government or donor-sponsored NGO which subsidizes the network<sup>25</sup>. Six interventions were identified, “Green Star” and “Green Key” in Pakistan, “Ray of Hope” in Ethiopia, “Janani” in Bihar State, India, “Sewa” in Nepal and “Top Réseau” in Madagascar. Evidence of impact on utilization or quality of health services was mixed. The Nepali study examined client satisfaction with quality of care. Clients at intervention clinics ‘very satisfied’ with cleanliness increased from 37% to 65%, and with the availability of essential equipment from 35% to 62%. Clients were also reported to be more satisfied with the range of services offered in the intervention clinics (40% to 71%) and with privacy (38% to 72%)<sup>26</sup>.

The Top Réseau study reported that coverage of modern contraceptives was higher for women with high exposure to the intervention (have accessed a franchised clinic and have been exposed to the IEC activities) than those with low or medium exposure<sup>27</sup>.

**5. Accreditation** is a strategy to improve and control the quality of services provided at organizational or facility level through oversight by an independent quality control evaluation body which may be the government or an NGO. It may include training providers in standardized practices<sup>28</sup>. A network of accredited drug dispensing outlets (ADDO) was implemented in rural and peri-urban Tanzania. The accreditation process, managed by the Tanzania Food Drug Authority (TFDA), aimed to improve access to affordable and quality medicines and pharmaceutical services through training and supervision of outlet dispensing staff, outlet inspections, marketing

and public education. The proportion of unregistered drugs decreased in both intervention and control areas, from 26% to 2% in the former, and from 29% to 10% in the latter<sup>29</sup>.

**6.Training** interventions can take various forms including formal training sessions, vendor-to-vendor education, distribution of guidelines and job-aids. A study of the Ghanaian intervention to improve Sexually Transmitted Infection management at pharmacies, which evaluated outcomes using simulated clients, found that when offered treatment, 38% of simulated clients received appropriate oral medication at intervention pharmacies compared with 18% at control pharmacies. Counseling about partner notification was 40% in intervention pharmacies compared with 21% in control pharmacies, though no recommendation to use a condom was given at intervention pharmacies compared with 13% at control pharmacies<sup>30</sup>.

**7.Regulatory** interventions aim to set up and ensure adequate technical quality of the services provided<sup>31</sup>. They take the form of rules, enforcement systems and sanction mechanisms, and can be applied at the levels of health care provider, organization or facility. At the provider level regulation may include requirements for pre-service training, continuing education, licensing and certification of providers<sup>32</sup>. At the organizational or facility level, regulation may aim to control the location of facilities, their registration and minimum complement of staff or facilities<sup>31</sup>. In addition, consumer protection legislation may be used to oversee medical practices and influence provider behavior. Pharmaceutical market regulation aims to limit the availability of harmful drugs and unregistered products, minimize drug misuse, control the sale of specific drugs through prescriptions, and regulate drug manufacture and importation<sup>22</sup>. In Nepal, the pharmaceutical ban prohibited the export, import, local production, transportation, storage, sale and distribution of Analgin (an analgesic and antipyretic drug) and its combination products<sup>33</sup>. As a result, the proportion of retail outlets with Analgin decreased from 96.5% at baseline to 21.2% five months after the intervention and 0% sixteen months after<sup>33</sup>.

**8.Contracting out** is a purchasing mechanism used to acquire specified services of a defined quality at an agreed price from a specific private provider and for a specific period of time. Governments may purchase clinical or non-clinical services from private providers to complement public provision<sup>34</sup>. Where interventions employed a mix of strategies we classified them by the primary or main intervention, based on the emphasis given in the paper or report. Contracting-out of district hospitals to private-for-profit management was implemented in rural South Africa. Public hospitals had better structural quality of care but contracted hospitals had better quality of nursing care in maternity and medical/surgical wards than public hospitals, similar nursing management quality, and overall,

higher total nursing quality. No statistically significant differences in perinatal and maternal mortality rates were found between contracted and public hospitals<sup>35</sup>.

## Human resources

There is growing evidence that HR inputs are an important determinant of broader population-based outcomes such as maternal mortality<sup>36</sup>. The relationship between lack of pregnancy-related care and maternal death is well recognized<sup>37</sup>. It is widely believed that most maternal mortality is preventable with skilled obstetric care<sup>38, 39</sup>. Considering the scope of the problem, surprisingly little attention has been given to HR management in India. Studies in India have confirmed the importance of Skilled Birth Attendants (SBAs), showing an inverse relationship between distribution of trained birth attendants and maternal mortality ratios<sup>40</sup>.

India has human resources for health comparable to other low-income countries, with seven physicians and eight nurses per 10,000 populations. The public health care system, which provides the only health care access for the poor, has only two physicians and eight nurses per 10,000 populations<sup>41</sup>. This human resource shortfall extends across all categories in the system, including shortages of female health assistants (30%), specialized doctors (68%), nurses and midwives (41%), and radiographers (57%)<sup>42</sup>.

## Public-private partnerships to provide emergency obstetric care

In many rural and under-sourced areas, particularly at the district health system level, there is dearth of skilled care providers practicing within the public health system. In many of these areas, private sector facilities and practitioners that provide comprehensive essential obstetric care exist; often providing higher-quality services than public-sector services, but the poorest women cannot afford the fees, and thus cannot access these services<sup>43</sup>.

Public-private partnerships offer one potential solution. Such partnerships vary widely in structure and function, and can range in size and complexity from small collaborations with industry or mission hospitals to large collaborative efforts between governments and private NGOs or UN agencies. In public-private schemes, public funds may be used to fund the cost of private providers' services to strengthen health services. New or expanded provider networks, often with district health official input, improve coverage at low or no cost to the rural poor. There are many different types of public-private partnerships, many of which involve community partnerships with a broad range of civil society groups and health care professionals to galvanize communities and health systems for perinatal health<sup>44</sup>. Few public-private partnerships have addressed the provision of antenatal and/or obstetric care, or comprehensive essential obstetric care, and few have assessed birth outcomes in relation to changes in the system of care.

## **Role of Traditional birth attendants (TBAs) in Public-Private Partnership**

TBAs have a role in supporting women during labor but are generally not trained to deal with complications. TBAs are generally categorized as trained or untrained. Even so-called “trained TBAs” have often had a month or less of training and therefore cannot be defined as skilled attendants who should possess a minimum of skills, confidence and connectedness to the health system for management of complications. TBAs have often learned to assist births by apprenticeship to more experienced TBAs, often observing local traditions and customs, and may provide other postnatal services to women including caregiving and domestic chores. TBAs practice widely in many areas with poor access to facility-based care, and may be the birth attendant of choice even for women with access to facility-based care. *Anganwadi* workers play a very crucial role in linking the Below Poverty Line (BPL) beneficiaries with Empanelled Private Providers as they suggest opting for free institutional delivery under the scheme rather than choosing home delivery<sup>2</sup>. More recently, the government has been experimenting with community health workers called *accredited social health activists* (ASHA) to carry out a variety of health initiatives as part of the National Rural Health Mission<sup>45</sup>.

Two of the projects in the multi-country Mother Care Project described by Kwast et al.<sup>46</sup> included components to improve TBA skills. In rural Guatemala, TBAs were trained to recognize and promptly refer pregnancy/delivery/neonatal complications, while the project simultaneously improved the quality of care in health facilities by modifying health professionals’ attitudes towards TBAs and clients and implementing management protocols. In the intervention area, referrals from TBAs increased by 313% and perinatal mortality among referred women decreased from 22.2% to 11.8% ( $P = 0.003$ ). In Indonesia, a project by the University of Padjadjaran sought to improve referral by TBAs and provide comprehensive essential obstetric care in the West Java sub-district of Tanjunsari. Referrals to birthing centers by TBAs increased from 19% to 62%, and perinatal mortality declined from 47.7 to 35.8/1000 over 18 months

## **Role of Faith-based organizations (FBOs) in Public-Private Partnership**

The management and the clinical care provided by faith-based organizations FBOs are often of higher quality than that provided by government hospitals. Mission hospitals have several advantages including more resources (especially foreign exchange), greater access to expatriate staff especially for training, and more flexibility in hiring and managing staff and in procuring and managing medicines and supplies. Increased collaboration between governments and mission hospitals, particularly in underserved and rural areas, could improve availability and quality of obstetric services enough to meet MDG5 targets.

## **Limitations**

It has been argued that there is “evidence that effective public-private partnerships can increase access, improve equity, and raise quality of health services”<sup>[12]</sup> and that governments should “urgently engage with private stakeholders to facilitate increased private sector participation”<sup>47</sup>. However, the case that private sector interventions improve equity has not yet been clearly made<sup>48</sup>. Moreover, one might fear that working with private for-profit providers may disproportionately benefit the wealthier members of the community who can afford their charges, and thus exacerbate inequity<sup>49</sup>. There is a growing body of evidence that the care provided in certain setups of the private sector is often of low technical quality<sup>50</sup>.

Fee-for-service methods of reimbursement aggravate the geographical maldistribution of personnel and facilities, and the competition for scarce personnel resources aggravates the difference in the quality of the public and private services. Thus the growth in demand for these types of providers may be expected to increase inequality of access in these two respects. The potential expansion of medical scheme coverage is shown to be limited to well under 50% of the population, leaving the majority of the population without access to private sector health care. Even for members of the medical schemes, benefits are linked to income, thus clashing with the principle of equal care for equal need. The public funds needed to overcome financial obstacles to access to private providers could be more efficiently deployed by financing publicly owned and controlled health services directly. Taxation also offers the most equitable method of financing health services<sup>51</sup>.

The use of private health care providers in low- and middle-income countries (LMICs) is widespread and is the subject of considerable debate. It is argued that encouraging the use of such clinics by those who can afford to pay for them might not help to improve care available for the poorest population groups, which are an important priority for the government. Encouraging such providers to compete for government funding could, however, be desirable if the range of services presently offered, and those able to access them, could be broadened. However, the constraints to implementing such a system successfully are notable, and these are acknowledged. Even without such contractual arrangements, these companies provide an important lesson to the public sector that acceptability of services to users and low-cost service delivery are not incompatible objectives<sup>52</sup>.

Established private providers, especially nurses/midwives, have the potential to contribute to safe motherhood practices if they are involved in the care continuum. However, they have largely been overlooked by policy-makers in low-income settings. The private sector (mainly doctors) contributes to overprovision and high Caesarean section rates in settings where it provides care to wealthier segments of the population; such care is often funded through third-party payment schemes. In poorer settings, especially rural areas, private nurses/midwives and the

women who choose to use them are likely to experience similar constraints to those encountered in the public sector - for example, poor or unaffordable access to higher level facilities for the management of obstetrical emergencies.

Finally, attention is drawn to the dilemma resulting from the strengthening of the private health sector; while in the short term this can offer better care to more people on a racially non-discriminatory basis, in the long term, health care for the population as a whole may become more unequal and for those dependent on the public sector it may even deteriorate.

### **Chiranjeevi Yojana- A Milestone in Public-Private Partnership**

Following a series of consultations with both public and private stakeholders, the government developed a Public Private Partnership (PPP) called "Chiranjeevi Yojana" which realigned health system human resources by relocating obstetric gynecology services from the public sector to the private sector in Gujarat<sup>53</sup>.

The scheme was first pilot-tested in five predominantly rural districts, and then scaled up across the state. Under the scheme, the Gujarat Health & Family Welfare Department recruited providers who had postgraduate qualifications in obstetrics and gynecology; owned their own hospital with a labor room, operating theatre and blood bank; and had access to anesthesiology services. In return, the state reimbursed physicians approximately USD 40 per delivery. Rather than pay providers directly, the Chiranjeevi Yojana scheme distributed vouchers to all pregnant women living below the poverty line (approximately USD 9 to USD 14 per person per month). Eligible women could choose a local OB/GYN and exchange the voucher for delivery services, free medicines and transport reimbursement<sup>53, 54</sup>. Through November of 2007, "Chiranjeevi Yojana" enrolled 843 providers and provided for almost 143,000 deliveries.

Chiranjeevi Yojana is considered to be a successful PPP model and has also received a prestigious Asian Innovations Award by the Wall Street Journal. It has been claimed by the government that maternal as well as neonatal deaths have been substantially reduced under the scheme. While 642 maternal deaths might have been anticipated in the programme through then, only 31 were reported. Strikingly, only 454 infants died, against an expectation of 6561 in the absence of the programme. Even more impressive, Gujarat was able to deliver these results through the direct relocation of obstetric gynecology services from public to the private sector<sup>36</sup>. With success come some failures too. There were lacunae in its implementation too. Most of the 56 obstetricians registered for the scheme were located in Surat city. Thus no private nursing homes from remote areas had volunteered to be part of the scheme. Out of the registered 56 EPPs, very few had been active and performed deliveries

under the scheme. The majority of EPPs had taken the first installment of Rs. 15,000/- from the CDHO and had not performed the number of deliveries that were expected. It was noted that some EPPs only took "safe" cases of normal delivery and divert complicated cases to the public hospitals. Some EPPs demanded additional money from BPL beneficiaries, which clearly breaks the trust between them. Further, EPPs claim that many beneficiaries are not really BPL, despite holding a card. If this is the general scenario then the entire purpose of the scheme is defeated as complications requiring EmOC are the root cause of maternal mortality and not the "safe" cases that these EPPs are treating. Besides, the scheme may only end up shifting the problem – the management of cases requiring EmOC – to public providers.

### **Moral aspects of public-private partnership**

Within both publicly and privately financed health care systems different funding mechanisms have evolved, or have been proposed, to deal with the problem of 'moral hazard'. Moral hazard arises when financial incentives within the health care system lead to either inefficient demand for care by consumers or inefficient supply of care by providers. If the objectives of health care delivery are 'maintenance or improvement of health' and 'equal access for equal need' then charges of finance of care through health maintenance organizations both appear to be less favorable than 'free' care at the point of delivery whilst the latter is not necessarily more costly as a result. Research on other suggested alternatives is required, otherwise radical changes to health care financing will simply result in movement from one unproven system to another<sup>4</sup>.

### **Conclusion**

Achieving MDG5 – reducing maternal deaths and providing universal access to reproductive health – will require substantial health system reform in many developing countries. Most, like India, face acute human resource shortages – particularly in rural areas where the needs are often greatest. In order to be successful, policy-makers will have to leverage a wide spectrum of resources, both public and private, to address the health needs of their populations. Realigning human resources through thoughtful use of public private transfer, task shifting, and position enhancement may offer the best opportunity for achieving improved health outcomes for women and children in resource-constrained settings.

Within the purview of financial constraints of the public health system, private funding, public-private cooperation and effective budgeting may become significant. Motivation of health workers and community to effectively utilize public health care services sets an evolutionary process of referral and vertical linkage of health care system one way of addressing financial barrier to care is through effective health insurance coverage for the poor. Certain not-for-profit organizations provide health insurance cover

to its members and their families. For example, Vimo SEWA covers a total of 1,39,752 members in Gujrat.

Factors important to sustainable delivery of care include an enabling environment, assured payment mechanisms for providers, and good collaboration and communication between public and private partners. Projects are underway to reduce maternal and neonatal mortality through public-private partnerships to finance private provider care in rural areas, such as the Chiranjeevi Project in Gujarat State. Further well-designed interventions and evaluations are needed to evaluate the cost-effectiveness and sustainability of these approaches in efforts to prevent stillbirth in low-/middle-income countries.

From a systems perspective there is a need to strengthen the PHC and EmOC facilities. A primary health care centre needs to be supported by secondary and tertiary level health services providing EmOC. The current public health system, however, faces a number of challenges and is not being able to address these needs. Inadequate funding, lack of accountability and responsiveness and incongruence between available funding and requirements have affected the performance to a large extent. Attempts to address some of these issues have not produced satisfactory results.

To conclude, shortage of human resources in the health sector has been one of the most important barriers in achieving health related MDG-5. Since the private health sector is present as well as preferred in India, possible contributions through Public-Private Partnership models like Chiranjeevi Yojana should be considered. Policy-makers at the country-level need to map the health system and understand the nature and distribution of the private sector, and what influences it. This potential resource could then be mobilized to work towards the achievement of safe motherhood goals.

Antenatal health care to the weaker section of society is of primary concern for every Health Care industry. Public-Private Partnership in antenatal care and other fields of health delivery seems to offer considerable promise. Though there are various models for PPP, we need to select the best approach from each of the projects and map out a program which includes the crux from each of them. The project should be framed keeping in mind the target population, the scenario in the society, and the sources available. The outcomes of various interventions should be statistically measured and monitored at regular intervals to be able to compare the results of different ways of organising the health care system. This potential resource could then be mobilized to work towards the achievement of safe motherhood goals.

## References

1. Mavalankar D, Rosenfield A. Maternal Mortality in Resource-Poor Settings: Policy Barriers to Care. *Am J of Public Health*. Feb 2005; 95(2): 200-203.
2. Millenium Development Goals. Available at: [www.developmentgoals.org](http://www.developmentgoals.org) Washington: World Bank; 2007.
3. Aggarwal AK. Strengthening Health Care System in India: Is Privatisation the Only Answer? *Indian Journal of Community Medicine*. Vol.33, Issue 2, April 2008; 69-70.
4. Ovretveit J. Beyond the public-private debate: the mixed economy of health. *Health Policy*. 1996 Jan; 35(1): 75-93.
5. UNICEF India Statistics. [http://www.unicef.org/infobycountry/india\\_india\\_statistics.html](http://www.unicef.org/infobycountry/india_india_statistics.html)
6. WHO Maternal Mortality in 2000: Estimates Developed by WHO, UNICEF, and UNFPA <http://www.reliefweb.int/library/documents/2003/who-saf-22oct.pdf> [PubMed]
7. Mavalankar D, Vora K, Prakasamma M. Achieving Millennium Development Goal 5: is India serious? *Bull World Health Organ*. 2008;86:243-243A. doi: 10.2471/BLT.07.048454. [PMC free article] [PubMed] [Cross Ref]
8. Ministry of Health and Family Welfare Annual Report 2004. New Delhi: Government of India; 2004.
9. Acharya A, McNacmee P. Can Public-Private Partnership reduce Maternal Mortality? Assessing efforts made by the 'Chiranjeevi' scheme in Gujrat. Available at: [www.esocialsciences.com/Document113112009270.2739069.pdf](http://www.esocialsciences.com/Document113112009270.2739069.pdf)
10. Makinen M, Waters H, Rauch M, Almagambetova N, Bitran R, Gilson L, McIntyre D, Pannarunothai S, Prieto AL, Ubilla G, Ram S. Inequalities in health care use and expenditures: empirical data from eight developing countries and countries in transition. *Bull World Health Organ*. 2000;78:55-65. [PMC free article] [PubMed]
11. Hotchkiss DR, Rous JJ, Karmacharya K, Sangraula P. Household health expenditures in Nepal: implications for health care financing reform. *Health Policy Plan*. 1998;13:371-383. doi: 10.1093/heapol/13.4.371. [PubMed] [Cross Ref]
12. Patouillard E, Goodman CA, Hanson KG, Mills AJ. Can working with the private for-profit sector improve utilization of quality health services by the poor? A systematic review of literature. *Int J Equity Health*. 2007; 6:17.
13. Kikumbih N, Hanson K, Mills A, Mponda H, Schellenberg JA. The economics of social marketing: the case of mosquito nets in Tanzania. *Soc Sci Med*. 2005;60:369-381. doi: 10.1016/j.socscimed.2004.05.005. [PubMed] [Cross Ref]
14. Mills A, Brugha R, Hanson K, McPake B. What can be done about the private health sector in low-income countries? *Bull World Health Organ*. 2002;80:325-330. [PMC free article] [PubMed]
15. Van Rossem R, Meekers D. An evaluation of the effectiveness of targeted social marketing to promote adolescent and young adult reproductive health in Cameroon. *AIDS Educ Prev*. 2000;12:383-404. [PubMed]
16. Paulino LS, Angeles-Agdeppal I, Etoroma UM, Ramos AC, Cavalli-Sforza T. Weekly iron-folic acid



- supplementation to improve iron status and prevent pregnancy anemia in Filipino women of reproductive age: the Philippine experience through government and private partnership. *Nutr Rev.* 2005;63:109–115. doi: 10.1301/nr.2005.dec.S109-S115. [Cross Ref]
17. Abdulla S, Schellenberg JA, Nathan R, Mukasa O, Marchant T, Smith T, Tanner M, Lengeler C. Impact on malaria morbidity of a programme supplying insecticide treated nets in children aged under 2 years in Tanzania: community cross sectional study. *BMJ.* 2001;322:270–273. doi: 10.1136/bmj.322.7281.270. [PMC free article] [PubMed] [Cross Ref]
  18. Marek T, O'Farrell C, Yamamoto C, Zable I. African Region Human Development Working Paper. Washington, DC, The World Bank; 2005. Trends and Opportunities in Public-Private Partnerships to Improve Health Service Delivery in Africa.
  19. Mushi AK, Schellenberg JR, Mponda H, Lengeler C. Targeted subsidy for malaria control with treated nets using a discount voucher system in Tanzania. *Health Policy Plan.* 2003;18:163–171. doi: 10.1093/heapol/czg021. [PubMed] [Cross Ref]
  20. Nathan R, Masanja H, Mshinda H, Schellenberg JA, de Savigny D, Lengeler C, Tanner M, Victora CG. Mosquito nets and the poor: can social marketing redress inequities in access? *Trop Med Int Health.* 2004;9:1121–1126. doi: 10.1111/j.1365-3156.2004.01309.x. [PubMed] [Cross Ref]
  21. Schellenberg JR, Abdulla S, Nathan R, Mukasa O, Marchant TJ, Kikumbih N, Mushi AK, Mponda H, Minja H, Mshinda H, Tanner M, Lengeler C. Effect of large-scale social marketing of insecticide-treated nets on child survival in rural Tanzania. *Lancet.* 2001;357:1241–1247. doi: 10.1016/S0140-6736(00)04404-4. [PubMed] [Cross Ref]
  22. SARA Toolkit to Improve Private Provider Contributions to Child Health. Washington, DC, USAID; 2005.
  23. Jacobs B, Kambugu FS, Whitworth JA, Ochwo M, Pool R, Lwanga A, Tiffit S, Lule J, Cutler JR. Social marketing of pre-packaged treatment for men with urethral discharge (Clear Seven) in Uganda. *Int J STD AIDS.* 2003;14:216–221. doi: 10.1258/095646203762869250. [PubMed] [Cross Ref]
  24. Brieger WR, Salako LA, Umeh RE, Agomo PU, Afolabi BM, Adeneye AK. Promoting pre-packaged drugs for prompt and appropriate treatment of febrile illnesses in rural Nigerian communities. *Int Q Community Health Educ.* 2003;21:19–40. doi: 10.2190/ON5X-ONVD-R0VB-4QKF. [Cross Ref]
  25. Montagu D. Franchising of health services in low-income countries. *Health Policy Plan.* 2002;17:121–130. doi: 10.1093/heapol/17.2.121. [PubMed] [Cross Ref]
  26. Agha S, Karim AM, Balal A, Sossler S. A quasi-experimental study to assess the performance of a reproductive health franchise in Nepal. Washington, DC, Commercial Market Strategies; 2003.
  27. Plautz A, Meekers D, Neukom J. PSI Research Division Working Paper No 57. Washington, DC, PSI; 2003. The impact of the Madagascar TOP Réseau social marketing program on sexual behaviour and use of reproductive health services.
  28. Smith E, Brugha R, Zwi A. Working with private sector providers for better health care: an introductory guide. London, Options and LSHTM; 2001.
  29. Sigonda-Ndomondo M, Kowero O, Alphonse E, Mbwasiri R, Shirima R, Frankiewicz C, Taylor M, Heltzer N, Clark M. Accredited Drug Dispensing Outlets: A Novel Public-Private Partnership: December; Dar es Salaam. *Management Sciences for Health*; 2003.
  30. Adu-Sarkodie Y, Steiner MJ, Attafuaah J, Tweedy K. Syndromic management of urethral discharge in Ghanaian pharmacies. *Sex Transm Infect.* 2000;76:439–442. doi: 10.1136/sti.76.6.439. [PMC free article] [PubMed] [Cross Ref]
  31. Conteh L, Hanson K. Methods for studying private sector supply of public health products in developing countries: a conceptual framework and review. *Soc Sci Med.* 2003;57:1147–1161. doi: 10.1016/S0277-9536(02)00491-4. [PubMed] [Cross Ref]
  32. Waters H, Hatt L, Peters D. Working with the private sector for child health. *Health Policy Plan.* 2003;18:127–137. doi: 10.1093/heapol/czg017. [PubMed] [Cross Ref]
  33. Dange Chettri GB, Kafle KK, Karkee SB, Rajubhandari V, Humagain B. Proceedings of International Conferences on Improving Use of Medicines (ICIUM): 2004 March 30-April 2; Chiang Mai. Effect of regulatory intervention on drug availability in Nepal.
  34. Marek T, Diallo I, Ndiaye B, Rakotosalama J. Successful contracting of prevention services: fighting malnutrition in Senegal and Madagascar. *Health Policy Plan.* 1999;14:382–389. doi: 10.1093/heapol/14.4.382. [PubMed] [Cross Ref]
  35. Broomberg J, Masobe P, Mills A. To purchase or to provide? The relative efficiency of contracting out versus direct public provision of hospital services in South Africa. In: Bennett S, McPake B, Mills A, editor. *Private health providers in developing countries: serving the public interest?* London, Zed Books; 1997.
  36. Anand S, Barnighausen T. Human resources and health outcomes: cross-country econometric study. *Lancet.* 2004;364:1603–1609. doi: 10.1016/S0140-6736(04)17313-3. [PubMed] [Cross Ref]
  37. Harrison KA. Tropical obstetrics and gynaecology. 2. Maternal mortality. *Trans R Soc Trop Med Hyg.* 1989;83:449–453. doi: 10.1016/0035-9203(89)90243-5. [PubMed] [Cross Ref]
  38. Sundari TK. The untold story: how the health care systems in developing countries contribute to maternal mortality. *Int J Health Serv.* 1992;22:513–528. doi: 10.2190/91YH-A52T-AFBB-1LEA. [PubMed] [Cross Ref]

39. Thaddeus S, Maine D. Too far to walk: maternal mortality in context. *Soc Sci Med*. 1994;38:1091–1110. doi: 10.1016/0277-9536(94)90226-7. [PubMed] [Cross Ref]
40. World Health Organization Improving Maternal, Newborn and Child Health in the South-East Asia Region: India. Geneva: World Health Organization; 2005.
41. World Health Organization Country Health System Profile: India. Geneva: World Health Organization; 2008.
42. Staff Reporter Over 800 rural hospitals don't have a single doctor. *Thaindian News*. New Delhi; 2008.
43. Gill Z, Carlough M. Do mission hospitals have a role in achieving Millennium Development Goal 5? *Int J Gynaecol Obstet*. 2008;102:198–202. doi: 10.1016/j.ijgo.2008.04.003. [PubMed] [Cross Ref]
44. Strobino DM, Baldwin KM, Grason H, Misra DP, McDonnell KA, Liao M, Allston AA. The relation of FIMR programs and other perinatal systems initiatives with maternal and child health activities in the community. *Matern Child Health J*. 2004;8:239–249. doi: 10.1023/B:MACI.0000047422.87300.f7. [PubMed] [Cross Ref]
45. Satpathy SK, Venkatesh S. Human Resources for Health in India's National Rural Health Mission: Dimension and Challenges. *Regional Health Forum*. 2006;10:29–37.
46. Kwast B. Reduction of maternal and perinatal mortality in rural and peri-urban settings: what works? *Eur J Obstet Gynecol Reprod Biol*. 1996;69:47–53. doi: 10.1016/0301-2115(95)02535-9. [PubMed] [Cross Ref]
47. Forum on engaging the private sector in child health 30 November 2005 — 2 December 2005; Munyonyo Hotel, Kampala, Uganda.
48. Travis P, Cassels A. Safe in their hands? Engaging private providers in the quest for public health goals. *Bull World Health Organ*. 2006;84:427. doi: 10.2471/BLT.06.032755. [PMC free article] [PubMed] [Cross Ref]
49. Montagu D, Prata N, Campbell MM, Walsh J, Orero S. HNP Discussion paper: Reaching The Poor Paper No 11. Washington, DC, The International Bank for Reconstruction and Development and the World Bank; 2005. Kenya: Reaching the poor through the private sector - A network model for expanding access to reproductive health services.
50. Bennett S, Hanson K, Kadama P, Montagu D. Making Health Systems Work: Working Paper No 2. Geneva, World Health Organisation; 2005. Working with the non state sector to achieve public health goals.
51. Price M. The consequences of health service privatization for equality and equity in health care in South Africa. *Soc Sci Med*. 1998; 27(7): 703-16.
52. Palmer N, Mills A, Wadee H, Gilson I, Schneider H. A new face for private providers in developing countries: what implications for public health? *Bull World Health Organ*. 2003; 81(4): 292-7.
53. Singh A, Mavalankar D, Desai A, Patel S, Shah P. Human resources for comprehensive EmOC: an Innovative partnership with the private sector to provide delivery care to the Poor. Ahmedabad: Indian Institute of Management, Ahmedabad; 2007. <http://gujhealth.gov.in/Chiranjeevi Yojana/pdf/Chiranjeevi Yojana-A Journey to safe motherhood.pdf>
54. Bhat R, Chandra P, S M. Involving Private Healthcare Providers to Reduce Maternal Mortality in India: A Simulation Study to Understand Implications on Provider Incentives. 2007. [http://www.iimahd.ernet.in/publications/data/2007-01-01\\_SMukherjee.pdf](http://www.iimahd.ernet.in/publications/data/2007-01-01_SMukherjee.pdf)

# Syndromic approach as an index of prevalence of sexually transmitted Infections in hills of Northern India

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## Introduction

Sexually transmitted infections (STIs), including human immunodeficiency virus (HIV), are imposing an increasing burden not only on public health but also on the world's economies, especially those of developing countries. According to an estimate by the World Health Organization (WHO), nearly a million people acquire STI, including HIV, every day. [1] All these infections cause 17% of economic losses for developing countries, which is a significant burden.[1] Failure to diagnose and treat STIs at an early stage may result in serious complications and sequelae and an increase in medical cost.[2,3] In order to respond to the need of STI prevention and treatment, especially in countries with limited resources, the syndromic diagnostic approach based on treatment of symptoms without laboratory confirmation was recommended by WHO.[4] This syndromic approach remains the key component of the most recent WHO guidelines.[3] Rather than relying on aetiological laboratory diagnosis, which requires relatively sophisticated laboratories, the syndromic approach is based on the identification of consistent groups of symptoms and easily recognized signs,[3] which is more practical and feasible for resource-limited settings. The present study was aimed to determine the prevalence of STIs in adult population (15-49 years) keeping in view the utility of diagnosing presence of STI on the bases of syndromic approach.

## Background

Himachal is situated in the western Himalayas. Covering an area of 55,673 kilometers (34,594 mi) this mountainous state has elevation ranging from about 350 meters (1,148 ft) to 6,000 meters (19,685 ft) above the sea level. There is great variation in the climatic conditions of Himachal due to extreme variation in elevation. The climate varies from hot and sub-humid tropical in the southern tracts to cold, alpine and glacial in the northern and eastern mountain ranges with more elevation. The population of Himachal in 2001 stood at 60,77,900 as per the provisional

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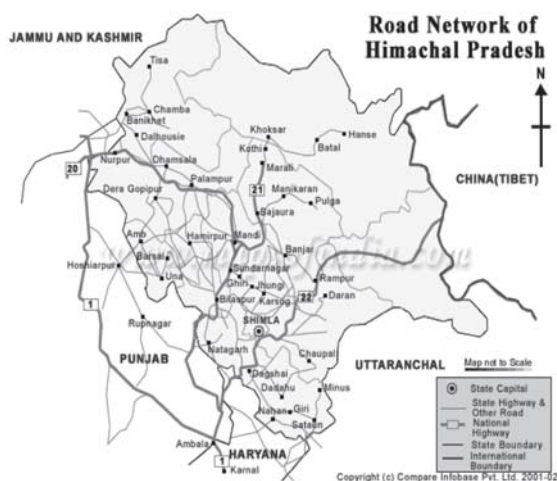
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results of the Census of India 2001, with a rural population of 54,32,319. The sex ratio (i.e., the number of females per thousand males) of population was recorded as 970, which has declined from 976 in the previous census. [5]

## Material and methods

The study was conducted among both male and female population aged 15-49 years in Shimla district of Himachal Pradesh. The district was identified into two broad areas, rural and urban. Shimla city was identified as the urban area for the study and the area around Shimla city was identified as the rural area for the study. By simple random technique the rural population was identified to be represented by Community Development Block, Kusumpati - Mashobra block of Shimla district. It was done in the framework of a single centre cross-sectional survey with sample size of 2000 individuals. The sample was calculated assuming a prevalence of 5% and an acceptable error of 20%. The sample was drawn by simple random sampling technique. The sample was drawn from rural area using multistage random sampling technique. In urban area out of 25 wards of Shimla Municipal Corporation, five wards were selected randomly.

For this study two performas were evolved separately for males and females. These were pretested on 50 individuals of both sexes in Shimla district independent of the survey population. The total sample size of 2000 was equally allocated to the urban and rural area. Each selected ward in urban area was allocated a sample of 200 whereas in sub-centres village the number was 100. In the selected

village/ward, all households were enlisted. First household was randomly selected using random number table. The study was started from this household. After completing the first household the subsequent household was visited till the required number was completed.

For the purpose of study the symptomatic men and women were categorized into six syndromes as per standard guidelines of National AIDS control organization.(6) These syndromes were: Vaginal discharge in females and urethral discharge in males, inguinal bubo, and Genital ulcer disease, Lower abdominal pain in females and scrotal swelling in males. Any male or female who had symptoms on history taking for the presence of one or more above syndromes was considered positive for that syndrome. For the purpose of study the following syndromes (6) were considered for the analysis:

### 1. Vaginal discharge

The patient complaining of vaginal discharge was examined for colour, consistency, odour and amount of discharge. Risk assessment was done as per the recommendation of National Aids Control Organisation. (6)

### 2. Urethral discharge

The presence of discharge from the urethra of male patient spontaneously or on milking the urethra.

### 3. Genital ulcer

Presence of an ulcer(s) in the genital region with or without associated lymphadenopathy

### 4. Lower abdominal pain

The complaint of lower abdominal pain in a woman which is accompanied by the presence of abnormal vaginal discharge, temperature more than 38°C and pain on moving the cervix.

## 5. Inguinal bubo

The complaint of enlarged and / or painful inguinal lymph nodes.

## 6. scrotal swelling

The complaint of swollen and / or painful scrotum not due to trauma.

Informed consent of the subject was taken. No hazardous procedure was carried out. Confidentiality of information was made in accordance with the principle embodied in the declaration of Helsinki and International Guidelines for Ethical Review of Epidemiological Studies.

## Results

The Study was carried out in five wards of Shimla Corporation representing the urban population and villages of ten sub-centres of Kusumpati - Mashobra which is a part of district Shimla representing the rural population. The age group of population ranged from 15-49 years with 952(47.6%)males and 1048(52.4%) females. There was not much difference in male and female population representing urban and rural areas. Majority of the population both in males (36.2%) and females(36.4%) were in the age group of 30-39 years with the mean age of 31 years and 30.1 years in males and females respectively.

A significantly ( $p < 0.0001$ ) higher prevalence was found between the age group 20-29 years. The prevalence was almost similar before and after this age group. In case of females a higher prevalence of 43.6% was found in the age group of 20-24 years, as compared to males in the same group, which was highly significant ( $p < 0.0001$ ). The prevalence was lower after the age of 25 years and after the age of 29 years the prevalence further declines. When the prevalence of various syndromes relating to STIs was

**Table 1:** Prevalence of STIs based on syndromic approach according to age.

Age Groups (Years)	Males			Females			Males & Female		
	Total No.	STIs Cases		Total No.	STIs Cases		Total No.	STIs Cases	
		No.	%		No.	%		No.	%
15-19	121	3	2.4	136	9	6.6	257	12	4.7
20-24	128	11	8.6	142	62	43.6	270	73	27.0
25-29	186	16	8.6	207	72	34.8	393	88	22.4
30-39	344	8	2.3	381	134	35.1	725	142	19.6
40-49	173	5	2.9	182	40	21.9	355	45	12.7
Total	952	43	4.5	1048	317	30.2	2000	360	18.0

Males Vs Females in 20-24 years age group  $\chi^2 = 136.9$  df = 1  $p < 0.0001$

**Table 2:** Prevalence different syndromes (STI) in males

STISyndrome	n=952	
	No.	%
Urethral discharge	28	2.9
Scrotal swelling	4	0.4
Inguinal bubo	3	0.3
Genital ulcer	8	0.9
Total	43	4.5

**Table 3:** Prevalence of various syndromes (STI) in females.

STISyndrome	N=1048	
	No.	%
Vaginal discharge	144	13.7
Lower abdominal pain	152	14.5
Inguinal bubo	5	0.5
Genital ulcer	16	1.5
Total	317	30.2

analyzed it was found that urethral discharge among males was most common syndrome. Among female respondent prevalence of vaginal discharge and lower abdominal pain was almost similar. However the prevalence of genital ulcer disease was more in females (15%) as compared to, 0.9% in male respondents.

## Discussion

Historically, the syndromic approach has been regarded as a simple and effective approach for STI Control, particularly in resource-poor settings where laboratory assessments are not available.

However, the utilization of a syndromic approach should be specific to the setting, with

Consideration of different populations, STI epidemics, disease types and capacity of health-care

workers. In order to assess the effectiveness of the syndromic approach, it is necessary to carry out

regular evaluations of the accuracy of diagnoses and patient satisfaction. At the same time, cheaper

and more effective laboratory approaches for STI diagnosis are required to ensure quality of care in

STI clinics in resource-poor settings. A study by Bosu (1999) has identified several advantages of the

syndromic approach, including the simplicity of its implementation, rapid diagnosis and treatment,

savings on the cost of laboratory tests, broader coverage and lower requirements for existing health

systems. [7] Several studies have also demonstrated the efficacy of the syndromic approach. [7-10]

The syndromic approach gave us an overall prevalence of 18% based on the presence or absence

of various syndromes identified for carrying out the study . The prevalence was 30.2% in females, as

compared to 4.5% in males. Syndromic approach seems to be a easy and effective way of

estimating the prevalence of STI in community as the results of the present study are comparable

with the studies conducted earlier in similar population settings.[11] The prevalence of STIs in our

study although lower in comparison to similar study conducted in Hamirpur district of Himachal

Pradesh(23.9%) but the prevalence of STIs among the females was higher in our study, as compared

to 26.2% found in that study. The variation may also be due in fact to that their study was

conducted among high risk population group.

Majority of STIs cases in our study were in age group of 20 – 29 years age group in males as well as

in females . This is comparable to the most of the studies conducted in developed and developing

countries [11,12,13,14,15] again an indicator of the effectiveness of picking cases of STI by

syndromic approach.

## References

1. World Health Organization. *Global Strategy for the Prevention and Control of Sexually Transmitted Infection: 2006–2015*.
2. La Ruche G, Lorougnon F, Digbeu N. Therapeutic algorithms for the management of sexually transmitted diseases at the peripheral level in Cote d'Ivoire: assessment of efficacy and cost. *Bull World Health Organ*. 1995; 73:305–313
3. World Health Organization. *Guidelines for the Management of Sexually Transmitted Infections: 2003*.
4. World Health Organization. *Management of Patients with Sexually Transmitted Disease. World Health Organization Technical Report Series 810*. Geneva: World Health Organization; 1991.
5. Population Census 2001. <http://himachal.nic.in/tour/census.htm>
6. National AIDS Control Organisation. Simplified STI and RTI treatment guidelines. NACO, ministry of health and family welfare, Govt. of India.
7. Bosu WK. Syndromic management of sexually transmitted diseases: is it rational or scientific? *Trop Med Int Health*. 1999; 4:114–119.
8. Liu H, Jamison D, Li X, et al. Is syndromic management better than the current approach for treatment of STDs in China? Evaluation of the cost-effectiveness of syndromic management for male STD patients. *Sex Transm Dis*. 2003; 30:327–330.
9. Mukenge-Tshibaka L, Alary M, Lowndes CM, et al. Syndromic versus laboratory-based diagnosis of cervical infections among female sex workers in Benin: implications of nonattendance for return visits. *Sex Transm Dis*. 2002; 29:324–330.
10. Pettifor A, Walsh J, Wilkins V, et al. How effective is syndromic management of STDs? A review of current studies. *Sex Transm Dis*. 2000; 27:371–385.
11. Sharma DP, Sharma TD, and Bhardwaj AK. A study report by Himachal Pradesh AIDS cell on Sexually Transmitted Infections.
12. Singh KK, Bloom S, Tsui AD 1998. Husbands reproductive health knowledge , attitude and behaviour in Uttar Pradesh, India. *Studies in Family Planning*. Dec. 1998; 29: 29-35.
13. Chopra A, Mittal R. Vaginitis and vaginal Flora. Study of 100 cases. *Indian J sex Transm Dis* 1993; 52-54.
14. R. A. Bang, M. Baitule, S. Sarmukaddam, A. T. Bang, Y. Choudhary and O. Tale. High Prevalence of gynaecological diseases in rural Indian women. *The Lancet* 1989; 333 (8629): 85-88.
15. Andersson-Ellstrom A, Forsmann L, Milson I. Age of sexual debut related to life-style and reproductive health factors in a group of Swedish teenage girls. *Acta Obstetricia et Gynaecologica Scandinavica*. 1996; 75(5); 484-489.

# Role of fundus biomicroscopy, photography & fluorescein angiography in evaluation of diabetic retinopathy in newly diagnosed diabetics: A prospective study

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## Introduction

Diabetes is a carbohydrate metabolic disorder caused by lack of insulin or resistance to insulin that results in increased blood glucose concentration known as hyperglycaemia & involves almost every system of body especially eye, kidney, nerves & blood vessels.

All diabetics are classified into two categories as type I, which is known as insulin dependent diabetes mellitus (IDDM) and type II, which is insulin dependent (NIDDM). The presentation of diabetes is variable; it may be either with classical sign & symptom of diabetes attributable to an osmotic diuresis, or may found accidentally, or may present with the complication involving the other systems. Accurate data concerning its prevalence & severity of retinopathy should be available, so that a well coordinated planning can be formulated and proper approach can be instituted to avoid its complication in the public health programme.

## Material & methods

This prospective case controlled randomized study was performed in department of ophthalmology L.L.R.M. Medical college Meerut, India on patients of newly diagnosed diabetes mellitus from October 2006 to March 2007. The study was started only after taking permission from the institutional ethical committee. All the patients of diabetes in the age group 0yr to 90 years were included in this study. The inclusion criteria were all the patients of confirmed diabetes. Patients in which fundus was not visible like dense cataract or vitreous haemorrhage or patients which are already under treatment for diabetic retinopathy were excluded from this study. Informed consent was taken from all the patients. The aim of this study was to evaluate the diabetic retinopathy in newly diagnosed patient.

Diagnosis of DM was made according to WHO criteria in Medicine Dept. of L.L.R.M. Medical College, Meerut on the basis of following criteria-

1. Symptoms of DM+ Random blood glucose conc.  $\geq 11.1$  mmol/Lt. (200mg %), OR
2. Fasting Plasma Glucose  $\geq 7$  mmol/Lt. (126mg %), OR
3. Two hr. Plasma Glucose  $\geq 11.1$  mmol/Lt. (200mg %) during oral TT.

After confirming diabetes, patient were examined for best corrected visual acuity, Slit lamp biomicroscopy with +90D lens, Color fundus photograph and Fluorescein Angiography.

Total 623 patients were examined in Ophthalmology Dept. of L.L.R.M. Medical College, Meerut. Level of Diabetic Retinopathy was defined according to the Early Treatment Diabetic Retinopathy Study Report No-12

## Observations

**Table 1:** showing distribution of patient (623) according to type of diabetes

Type of diabetes	no of patient	percentage%
Niddm	548	88.14
Iddm	75	11.86
Total	623	100%

**Table 2:** Showing percentage distribution of retinopathy in newly diagnosed patient (623)

Type of diabetes	total no of patient	patient with retinopathy	%
Niddm	548	115	20.9
Iddm	75	2	2.6
Total	623	117	18.7

**Table 3:** showing Sex wise distribution of cases (n=117)

Sex	No. of patient	%
Male	56	47.86
Female	61	52.14
Total	117	100%

**Table 4:** showing Age wise distribution of cases (n=117)

Age (yr)	No. of cases	%
0-10	—	—
11-20	—	—
21-30	4	3.42
31-40	8	6.84
41-50	45	38.46
51-60	53	45.29
61-70	6	5.13
71-80	1	0.85
81-90	—	—

After completing the study we observed that Maximum newly diagnosed patients lie in the age group of 51-60yrs (table.4). There is no significant male-female differentiation (table.3). Out of 623 newly diagnosed patients 88.14% patients belonged to NIDDM & only 11.86% were of IDDM (table.1). In 548 newly diagnosed patients of NIDDM 20.9%

**Table 5A:** showing Distribution of NIDDM (115 out of 548) cases acc. to level of Retinopathy

Level of Retinopathy	No. of cases	%	Associated macular oedema
NPDR	106	19.3	6
PDR	9	1.6	---

**Table 5B:** showing Distribution of NIDDM (115 out of 548) cases acc. to level of Retinopathy

Level of Retinopathy	No. of cases	%	Associated macular oedema
NPDR	106	19.3	3(0.54)
Mild	99	18.06	3(0.54)
Moderate	5	0.91	---
Severe	2	0.36	---
Very severe	-	---	---
PDR	9	1.6	3(0.54)
Early	9	1.6	3(0.54)
High risk	-	---	---

**Table 6:** showing Distribution of Macular oedema

Type of Macular Oedema	No. of cases
Diffuse	2
Ischemic	---
Focal	4

**Table 7:** Showing Distribution of IDDM (75) cases acc. to level of Retinopathy

Level of Retinopathy	No. of cases	%	Associated macular oedema
NPDR	2	2.6	---
Mild	2	2.6	---
Moderate	---	---	---
Severe	---	---	---
Very severe	---	---	---
PDR	0	0	0
Early	---	---	---
High risk	---	---	---

had retinopathy out of which mild NPDR was seen in 18.06%, moderate in 0.91% & severe in 0.36% while early PDR was seen in 1.6%(table.5A&5B) . Only 6 patients had macular oedema in NIDDM cases (548) & were associated more with early PDR (table.6). In 75 newly diagnosed patients of IDDM 1.5% had retinopathy & all patients had mild grade NPDR (table.7)

## Discussion

The fluorescein angiography delineates the micro vascular structure in detail to show the pathological changes seen only by histopathologists in past. Many fundus changes are incapable to explain the symptom. Fluorescein angiography is a step towards these unexplained problems. A discrete population of patients with fundus changes has been studied by fluorescein angiography to objectively analyze the subtle or hidden information. So,

the present study is to evaluate the role of fluorescein angiography in various retinal disorders. The conclusions were drawn that, In Diabetic retinopathy male & female were equally affected. All cases were observed between 31-40 years of age with peak incidence in 51-60 years age group. Macular oedema was associated with every level of retinopathy& proliferative diabetic retinopathy had maximum no. of macular oedema cases (75%). On the basis of fluorescein angiography only 44.8% cases of macular oedema were treatable. All cases of macular oedema with Mild NPDR were treatable. So FA is a very good diagnostic tool in almost all cases of DR. It should be done in almost every case to diagnose even subtle cases of retinopathy because only by fundus examination it is impossible to rule out retinopathy.

## References

1. Amalric P: New developments in fluorescein angiography. *Doc Ophthalmol.* 43:125-35, 1977.
2. Ausberger JJ, Coats TD, Lauritzen K: Localized supra-choroidal hemorrhages: ophthalmoscopic features, fluorescein angiography, and clinical course. *Arch Ophthalmol* 108:968-972, 1990.
3. Bresseler NM, Bresseler SB, Alexander J, et al: Loculated fluid. A previously undescribed Fluorescein angiographic finding in choroidal neovascularisation associated with macular degeneration. *Arch Ophthalmol* 109:211-215, 1991.
4. Brown GC, Magargal LE: The ocular ischemic syndrome. Clinical, fluorescein angiographic and carotid angiographic features. *Int Ophthalmol* 11:239-251, 1988.
5. Butner RW, Mcpherson AR: Adverse reactions in intravenous fluorescein angiography. *Ann Ophthalmol* 15:1084-1086, 1983.
6. Chamberlin JA, Bresseler NM, Bresseler SB, et al: The use of fundus photographs and Fluorescein angiograms in the identification and treatment of choroidal neovascularisation in the macular photocoagulation study. *Ophthalmology* 96:1526-1534, 1989.
7. Chao P, Flocks M: the retinal circulation time. *Am. J. Ophthalmol.* 46:8-10, 1958.
8. Chopdar S: Retinal telangiectasis in adults: Fluorescein angiographic findings and treatment by argon laser. *Br J Ophthalmol* 62:243-250, 1978.
9. Choromokos EA, Wilson CA, Raymond LA, Lipman MJ: fluorescein angiography using ultra-high speed film. *Ann. Ophthalmol.*, 22, 299-301, 1990.
10. Cunningham E. E., Balu V. Cardiac arrest following fluorescein angiography. *JAMA* 242, 2431, 1979.
11. David NJ, Norton EWD, Gass JD, Beauchamp J: fluorescein angiography in central artery occlusion. *Arch Ophthalmol* 77:619-629, 1967.
12. de Venecia G: Fluorescein angiographic smoke stake. Case presentation at Verhoeff Society Meeting. Washington, DC, April- 2 25, 1982.

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