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# Screening for Nasal Colonizers: Mandatory to Prevent Surgical Site Infections

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## Abstract

**Background:** The current study examines the impact of best practices and active surveillance screening for nasal colonizers on reduction of post-surgical infections.

**Aim:** The aim was to study the prevalence of multi antibiotic resistant commensal bacteria in a healthy population.

**Materials and Methods:** Nasal swabs of 100 outpatients attending surgical department were collected aseptically and cultured using standard microbiological protocols. Antibiotic susceptibility was done by Kirby-Bauer disc diffusion method according to Clinical and Laboratory Standards Institute guidelines.

**Results:** Of 100 samples, 96 isolates were obtained. Eighty isolates were *Staphylococcus* species of which *Staphylococcus aureus* 42 (43.75%), coagulase negative *Staphylococcus* (CONS) (10.4%), methicillin resistant *S. aureus* (10.4%) and methicillin resistant CONS (18.75%) and among Gram-negative bacteria *Escherichia coli* (12.5%) and *Klebsiella* (4.16%). Multi-antibiotic resistance was seen among 30 (37.5%) of the total *Staphylococcus* species isolated and 3 (16.66%) among Gram-negative bacteria.

**Conclusion:** In the era of multidrug resistance, screening anterior nares in pre-surgical patients is an easy method to tackle resistant pathogens. At community level, this high percentage of resistant bacteria is quite alarming for us to take appropriate measures.

**Keywords:** Methicillin resistant *Staphylococcus aureus*, Nasal colonizers, Surgical site infections

## INTRODUCTION

Colonization with multi antibiotic resistant bacteria is a common problem in India. Nasal colonization with multi-drug resistant (MDR) bacteria plays a pivotal role in increasing the prevalence of community-acquired infections worldwide. There is a lot of evidence that these infections are spreading among healthy individuals. We have known that community-acquired infections can become a source of infection at hospital admission, especially for those patients who are intending to undergo any surgery.

Nasal carriage of bacteria acts as endogenous reservoir for clinical infections in the colonized individual, but also as a source of cross-colonization for community spread. The spread of colonization occurs especially in close contact areas such as schools, pre-schools or households.<sup>1</sup> The

individuals colonized with bacteria such as methicillin resistant *Staphylococcus aureus* (MRSA), -MDR Gram-negative bacteria tend to have complicated the clinical course from a disease originating from their endogenous sources.<sup>2</sup> The complicated clinical course results from increasing resistance in isolates and also the bacteria can cause deep-seated infections and sepsis. The difficulties in treating these deep-seated infections and sepsis require urgent measures to prevent further spread of MDR bacteria.

Though for the last 50 years, the nose has been intermittently recognized and targeted as a source of pathogens causing surgical site infection (SSI),<sup>3</sup> centers for disease control and prevention guidelines do not make a recommendation for or against screening and decolonization before surgical procedures.<sup>4</sup> Setting up a bacterial surveillance system is one of the strategies to understand the epidemiology to

guide local antibiotic policy and to compare resistance patterns with other international surveillance systems. An improved understanding of epidemiology and resistance mechanisms of community acquired infections are required for designing better preventive strategies for further spread of resistance in India, studies have been done in adults in intensive care units and among patients at high risk of infection, but studies on the prevalence of nasal carriage and antibiotic susceptibility pattern at the community level are few. Patients who are not hospitalized can be taken as a group to represent the community at large. Pre-operative colonization with any resistant bacteria is a well-established risk factor for post-operative SSIs. Today we are mostly worried about that hospital acquired infections, which infects after 72 h of hospitalization. We are neglecting the prevalence of community acquired infections, which can be a source of infection for post-operative SSIs. A regular surveillance system is important in ensuring quality of patient care, which reduces the mortality, morbidity and hospital stay. The present study is done to understand the epidemiology of nasal carriage of infections in view of the paucity of studies in a healthy community in India.<sup>5</sup> This study might be a helpful guide to know the prevalence of resistant commensal bacteria in a healthy population and also to predict that these bacteria can be the foci of infection in case of any surgeries.

## MATERIALS AND METHODS

The present study is a random cross-sectional study conducted during 2013 in the Department of Microbiology, Mysore Medical College and Research Institute and its attached hospitals, Mysore.

A total of 100 patients attending surgical outpatient department without any history of hospital admission in the previous 1 year were included in the study. An informed consent was obtained from the respective patients. Detailed personal histories about hypertension, diabetes, alcohol intake, smoking etc., were taken.

Subsequently, under aseptic conditions two nasal swabs were obtained from each patient. Total transit time to the laboratory was within 30 min. Samples were processed as per the standard protocol.<sup>6</sup> Microscopy and culture were done.

Anti-biotic susceptibility test (AST): AST was performed using Kirby Bauer's disk diffusion test as per Clinical and Laboratory Standards Institute guidelines.<sup>7</sup> Ampicillin - 10 mcg, erythromycin - 15 mcg, clindamycin - 2 mcg, cefoxitin - 30 mcg, vancomycin - 30 mcg, tetracycline - 30 mcg, chloramphenicol - 30 mcg, co-

trimoxazole - 23.75 mcg disks were used to test the antimicrobial susceptibility. Cefoxitin disk was used to identify methicillin resistance.<sup>7</sup> Based on coagulase test and cefoxitin disk screen test, strains were identified as methicillin sensitive *S. aureus*, MRSA, methicillin sensitive CONS and methicillin resistant CONS (MRCONS).

Ampicillin - 10 mcg, tetracycline - 30 mcg, gentamicin - 10 mcg, ciprofloxacin - 5 mcg, ceftazidime - 30 mcg, ceftazidime/clavulanic acid - 30/10 mcg, co-trimoxazole - 23.75 mcg and meropenem - 10 mcg disks were used to test the susceptibility in the Gram-negative bacteria.

The isolates resistant to three or more than three category of antimicrobials used for testing antimicrobial susceptibility pattern were considered as MDR bacteria.

## RESULTS

A total of 100 patients attending surgery outpatient were included in the study. Among them 70 were males, 30 were females. Age distribution of our study group is as depicted in Table 1. Out of 100 cases, history of smoking was present in 26 patients, alcohol intake was present in 20 patients, 6 patients had hypertension, and five had history of diabetes.

Of 100 samples, 96 isolates were obtained. Culture yielded no growth in 28 samples.

Among 100 patients, 58 patients were mono-bacterial carriers, and 14 were polybacterial carriers.

Different isolates obtained from nasal swabs are depicted in Table 2. Anti-biotic susceptibility pattern of each isolate is as shown in Table 3 and Table 4. Multi-anti-biotic resistance was seen among 30 (37.5%) of the total *Staphylococcus* species isolated and 3 (16.66%) among Gram-negative bacteria.

## DISCUSSION

Nasal colonization from decades has remained as a silent threat in the spread of infections in the community as well as in the hospitals. Commensals which were non-pathogenic have acquired resistant genes, and also, pathogenic bacteria

**Table 1: Age distribution of the patients**

Age in years	Total number of cases (n=100) (%)
15-35	36 (36)
36-55	48 (48)
56-75	14 (14)
76 and above	02 (2)



**Table 2: Isolates obtained from nasal swabs**

Isolates	Total number of isolates n=96	Percentage
<i>S. aureus</i>	42	43.75
MRSA	10	10.40
CONS	10	10.40
MRCONS	18	18.75
<i>E. coli</i>	12	12.50
<i>Klebsiella</i> species	4	4.16

*S. aureus*: *Staphylococcus aureus*, MRSA: Methicillin resistant *Staphylococcus aureus*, CONS: Coagulase negative *Staphylococcus*, MRCONS: Methicillin resistant coagulase negative *Staphylococcus*, *E. coli*: *Escherichia coli*

**Table 3: Antibiotic resistance pattern of *Staphylococcus* isolates**

Antibiotics	<i>S. aureus</i> (n=42) (%)	MRSA (n=10) (%)	CONS (n=10) (%)	MRCONS (n=18) (%)
Ampicillin	36 (85.7)	9 (90)	10 (100)	16 (88.88)
Erythromycin	28 (66.66)	7 (70)	3 (30)	2 (11.11)
Clindamycin	22 (52.38)	8 (80)	4 (40)	4 (22.22)
Cefoxitin	0 (0)	10 (100)	0 (0)	18 (100)
Ciprofloxacin	14 (33.33)	3 (30)	2 (20)	9 (50)
Vancomycin	42 (42)	0 (0)	0 (0)	2 (11)
Tetracycline	12 (28.57)	7 (70)	3 (30)	3 (16.6)
Chloramphenicol	15 (35.71)	2 (20)	1 (10)	2 (11)
Cotrimoxazole	17 (40.47)	3 (30)	2 (20)	5 (27.77)

*S. aureus*: *Staphylococcus aureus*, MRSA: Methicillin resistant *Staphylococcus aureus*, CONS: Coagulase negative *Staphylococcus*, MRCONS: Methicillin resistant coagulase negative *Staphylococcus*

**Table 4: Antibiotic resistance pattern of Gram-negative organisms**

Antibiotics	Organism isolated (%)	
	<i>E. coli</i> (n=12)	<i>Klebsiella</i> (n=4)
Amoxycillin	10 (83.33)	3 (75)
Tetracyclin	8 (66.66)	2 (50)
Gentamycin	4 (33.33)	2 (50)
Ciprofloxacin	3 (25)	1 (25)
Ceftazidime	2 (16.66)	2 (50)
Co trimoxazole	3 (25)	2 (50)
Meropenem	0 (0)	1 (25)
Cefotaxime	2 (16.66)	2 (50)

*E. coli*: *Escherichia coli*

are replacing commensals. A community infection is an infection that was present or incubating at the time of admission and was not caused by an organism acquired during previous health care.

Our study has included 100 outpatients attending surgical department for some complaints. These patients do not have any previous history of hospital admission for past 1 year. Surgical outpatients were considered because these patients if at all are admitted for any surgeries, screening of anterior nares for resistant bacteria would be a useful guide for avoiding SSIs. The common age group in our study group was 15-55 years who showed more nasal colonization. This is significant because

majority of patients are in the working age group who are the major source of spreading infections in the community. Probably, more exposure, working environment, movements, educational status, ignorance, smoking, etc. can be the added reasons. There are no sex differences in the rate of colonization as we are living in the cosmopolitan society.

*S. aureus*, which is the most common nasal colonizer now poses a major threat because of acquiring resistance and becoming more virulent. *S. aureus* is a common pathogen responsible for community as well as hospital-associated infections worldwide. In our study, the rate of nasal colonization of *S. aureus* was 54.16% which is comparatively on the higher side than a study conducted on colonization of MRSA among health care workers in a tertiary care hospital of Delhi in the year 2002. In another study, nasal swabs taken from the healthy individuals in the community, 29.6% yielded growth of *S. aureus*.<sup>8</sup> The anterior nares have been shown to be the main reservoir of *S. aureus* in both adults and children. *S. aureus* strains may spread readily from colonized or infected persons. The *S. aureus* is transmitted to nares by contaminated hands and from surfaces where it can survive for months.<sup>2</sup> Health care workers can be one of the very important sources to carry these resistant bacteria to the general population. Colonization of the nares is a potent and increasingly prevalent risk factor for subsequent *S. aureus* infection.<sup>9</sup> In at least 80% of *S. aureus* bacteremia cases in colonized subjects, the infecting strain is identical to nasal colonizing strain detected prior to onset of bacteremia.<sup>10</sup> Increasing trends of *S. aureus* colonization in nares when compared to other studies is quite alarming. *S. aureus* is the most common nasal flora, which is an important risk factor for infection, especially deep-seated infections and septicemia.<sup>2</sup> Furthermore, we should look whether these isolates are just commensals or carrying any resistant genes. Hence, if at all if we can look for antibiotic susceptibility pattern of these isolates, we will be able to guide the clinicians about the resistant isolates.

MRSA is a major global problem. We have isolated 19.23% (10/52) MRSA strains and 64.28% (18/28) CONS were showing methicillin resistance in our study. In a study of healthy individuals, there is a report of 18.1% MRSA detection and among healthcare workers it is 25%. The study indicated the existence of MRSA even among the healthy population with no recent exposure to hospital or healthcare workers, although the isolation rate and resistance among healthcare workers was more. There is a growing urgency to study the colonization behavior of MRSA and MRCONS. Most of the CONS were showing sensitivity to other group of drugs except for cefoxitin, indicating the community acquired origin. This was proved

by the facts that the strains were obtained mainly from patients with no history of hospitalization in the last 1 year. Horizontal transfer of genes can happen between a hospital acquired MRSA to a community strain. However, we have to genotype the isolates to say exactly whether the strain is community acquired. Colonization rates of MRSA in the community have been reported to range from 0% to 9.2%.<sup>11</sup> Asymptomatic colonization can persist for months to years.<sup>12</sup> However, the potential for outbreaks of disease and spread of the pathogen to different niches like critical care units can cause havoc.<sup>13</sup> The sharp increase in the prevalence of MRSA acquired infections in many communities had led to the consideration of outpatients as a source of infection.<sup>14</sup>

Multi antibiotic resistance was seen among 30 (37.5%) of the total *Staphylococcus* species isolated and among Gram-negative bacteria 3 (16.66%). The risk factors for increased resistant *Staphylococcus* include overcrowding, visit to a local doctor, recent hospital checkup, history of diabetes, alcohol intake, hypertension recent visit to the hospital, and skin infection. Hospitalization, skin maceration and multiple needle prick injuries are the factors supposed to produce such increased colonization.<sup>2</sup> In healthy subjects over time, three patterns of carriage can be distinguished: About 20% of people are persistent carriers, 60% are intermittent carriers, and approximately 20% almost never carry *S. aureus*.<sup>2</sup> we could not evaluate that whether patients were transient colonizers or persistent carriers. Such carriers play a pivotal role in spreading the infections in the community and hospitals and also act as major sources of cross infections.

The poly bacterial carrier with resistant bacteria has become a matter of concern that are spread in the community. Lack of awareness, low levels of education, poor sanitation and hygiene are other contributing factors for the spread of infections. Pre-operative screening for nasal carriage and subsequent treatment of carriers with mupirocin and chlorhexidine reduces the risk for the development of *S. aureus* infections by 79% for deep-seated infections and 55% for superficial infections.<sup>15</sup> Consequently, the mean duration of hospital stay is reduced in treated carriers by approximately 2 days. The relative risk of SSI is 2-9 times greater in carriers of *S. aureus* than in non-carriers.<sup>2</sup> Furthermore, molecule are pidemiology has demonstrated that the strain of *S. aureus* that causes a post-operative infection is identical to the strain isolated from the nasal cavity pre-operatively in 85% of patients.<sup>16</sup> Thus, SSI due to *S. aureus* are due to endogenous microbes. Not surprisingly, nasal carriage of *S. aureus* is an independent risk factor for SSI in cardiac, vascular and orthopedic implant surgery.<sup>17</sup>

Unlike other studies which shows growth of only *Staphylococcus* strains, in our study there were *Escherichia coli* (12.76%) and *Klebsiella* (4.16%). This is a wakeup call to all the clinicians and microbiologists to widen their views about colonizing flora as these Gram-negative bacteria are versatile in causing infections and also are the established pathogens with their drug resistant patterns. We have further to evaluate to see whether these bacteria are resident or temporary colonizers.

Hence, forth screening patients to detect colonization by these organisms is used to determine specific interventions such as decolonization treatment, prophylactic antibiotics such as using mupirocin and chlorheximide (CHX) ointments prior to surgical interventions or for selection of empirical antibiotic therapy and to isolate patients, so that transmission of these difficult to treat organisms to other patients could be prevented. Detecting the nasal colonizers by means of simple cultures and battery of biochemical reactions prior to the procedures or operations and treating them with appropriate antibiotics prevent the cross infections. A cost-benefit analysis shows that the strategy is cost-effective and saves lives.<sup>18</sup> Thus in the era of dramatized increase in the antibiotic resistance, hospital and community acquired infections use of simple methods in identification, and subsequent prevention of nasal colonizers should be considered as a mandatory investigation before surgical interventions, thus reducing SSIs, morbidity and hospital stay. Achieving this attainable reduction in both morbidity and health care costs requires a combined effort of clinicians, laboratory, and hospital administration.

## CONCLUSION

Nasal colonization in our study showed multi-drug resistance which helps both the clinicians and microbiologists to broaden the views about nasal colonization and resistance patterns. Anterior nares screening should be a part of pre-surgical investigation. With the availability of identification of resistant bacteria in anterior nares, clinician can take a step towards reducing SSIs.

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# Prevalence of Urinary Tract Infection in Febrile Children below 5 Years of Age, Admitted in Tertiary Care Hospital in Dakshina Kannada District, Karnataka, India

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## Abstract

**Purpose:** Urinary tract infection (UTI) is a leading infection in pediatric patient causing morbidity and mortality. Normally, urinary tract proximal to distal urethra is sterile, but is constantly challenged by the infectious pathogens fighting to gain access. Vast majority of UTI's are caused by bacterial agents. *Escherichia coli* accounts for more than 80% of acute UTI in children. As urine contains urea, chronic infection with urea splitting organism such as *Klebsiella*, *Proteus* species may cause further complications in the patients leading to urinary calculi. Hence there is a need of early diagnosis of UTI in febrile pediatric patients to reduce morbidity and mortality, and to reduce the treatment burden on the patients.

**Materials and Methods:** Sample size-100: Informed consent was taken from all the subjects and this study was approved by Institutional Human Ethics Committee. Sample collected was mid-stream urine, and it was processed in the microbiology laboratory. Urine culture was done by semi-quantitative method in cysteine lactose electrolyte deficient agar media and quantitative unspun wet mount microscopy done to detect pyuria. Antibiotics sensitivity was put up by the Kirby Bauer method following the Clinical Laboratory Standards Institute guidelines.

**Result:** Growth was present in 35 patients ( $>10^5$  colony forming units/ml) i.e., in 21 boys out of 60 boys and 14 girls out of 40 girls taken for the study. In the culture *E. coli* was the predominant organism grown; it was 100% sensitive to a higher group of antibiotics and was completely resistant to ampicillin.

**Conclusion:** Our study revealed that *E. coli* is the most predominant organism grown in the culture, which indicates, most common bacteria causing UTI in the febrile children below 5 years of age is *E. coli* and then followed by *Klebsiella*.

**Keywords:** Antibiotics sensitivity, *Escherichia coli*, Urinary tract infection

## INTRODUCTION

Urinary tract infection (UTI) is a leading infection in pediatric patient causing morbidity and mortality. UTI can be defined by the presence of a significant quantity of bacteria in the urine along with signs and symptoms of infection.<sup>1</sup>

Normally, urinary tract proximal to distal urethra is sterile, but is constantly challenged by the infectious pathogens fighting to gain access. A UTI, strictly speaking, occurs when an infectious agent is present within this sterile

system, however, a more appropriate clinical definition is that UTI occurs when an infectious agent is not only present, but it is also causing illness.<sup>2</sup>

Throughout childhood, the risk of UTI is 2% for boys and 8% for girls. Inpatient admission is required in 2-3% of cases. UTI in pediatric patients is usually under-diagnosed in most of the primary care center's.<sup>2</sup>

The diagnosis of UTI is presumed when irritative urinary tract symptoms occurs simultaneously with the positive test for infectious agents such as bacteria, fungi, viruses



or parasites in the urinary tract. Because other factors can also cause similar symptoms, the presence of symptoms in the absence of positive culture has historically been considered inadequate for diagnosis.<sup>3</sup>

Similarly, the presence of leucocytes (pus cells) in urine is not a proof of infection.

Asymptomatic bacteriuria may represent colonization or contamination and should be differentiated from UTI.<sup>4</sup>

In pediatric patients, UTI presents with non-specific symptoms, making the diagnosis more confusing. If UTI is not diagnosed in the initial stage, it may lead to permanent renal damage and thereby leading to renal failure.<sup>4</sup>

Vast majority of UTI's are caused by bacterial agents. The bacterial pathogens causing UTI in pediatric age group are mainly the Gram-negative bacilli belonging to *Escherichia* ceae family, which are the colonizer of gastro intestinal tract. *Escherichia coli* accounts for more than 80% of acute UTI's in children.<sup>4</sup> As urine contains urea, chronic infection with urea splitting organism such as *Klebsiella*, *Proteus* species may cause further complications in the patients leading to urinary calculi.<sup>4</sup> Less common infectious agents include Gram-positive cocci, such as *Enterococcus* and *Staphylococcus*. Hence there is a need of early diagnosis of UTI in febrile pediatric patients to reduce morbidity and mortality, and to reduce the treatment burden on the patients. The incidence in neonates is 0.01-1% and can also be as high as 10% in low-birth weight and preterm neonates. Even children with a proven UTI deserve investigation, after first attack. However, care has to be taken not to expose the child to the excess investigation.<sup>4</sup>

UTIs can be categorized as complicated and uncomplicated. Complicated UTIs are infections in which there is a co-morbidity that predisposes a child either to infection or to a greater morbidity due to infection. Co-morbidities include presence of stones, neurological impairment affecting urinary tract functioning and anatomic abnormalities such as obstruction reflux or enterovesical fistula.<sup>4</sup>

Diagnostic work up should be modified to recognize any condition that leads to stasis of urine in the bladder. Renal calculi, obstructive nephropathy (posterior urethral valves), vesicoureteric reflux and voiding disorders can lead to urinary stasis and may predispose to the development of recurrent UTI and complications.<sup>5</sup>

Treatment of UTI is mainly by antibiotics. But, nowadays, many bacteria are developing resistance to most of the antibiotics. Empirical treatments with antibiotics are considered to be the main cause for the development of

resistance. Thus, it is important for a physician to treat the organism causing infection with antibiotics to which it is sensitive, after its sensitivity report is obtained.

### Review of Literature

The study aimed at determining age-stratified rates of co-existing bacterial meningitis in children with UTI, and it also aimed to determine the causative pathogens of UTI (Tebruegge *et al.*).<sup>5</sup>

Commonest organism isolated for all age groups, and gender was *E. coli* (74.5%) and *Klebsiella* (8.7%). Among oral antibiotics *Escherichia* family was most susceptible to amoxicillin/clavulanic acid (amoxycrav), there was a significant difference in susceptibility of common oral antibiotics when tested against the enterobacter for both male and female patients (Bahadin *et al.*).<sup>6</sup>

In a study conducted in Mwanza city, North western Tanzania, samples were obtained from the febrile children between 2 months and 5 years of age by urethral catheterization techniques in infants and pre toilet trained children to collect urine samples. For other group of children, a clean catch method of the mid stream urine was used to obtain samples. Urine samples were inoculated on the lactose electrolyte deficient agar McConkey and blood agar plates. Antibiotic sensitivity testing was done by disk diffusion method.

The high prevalence of resistance (97-100%) to ampicillin and amoxycrav. In addition, *E. coli* from urine was resistant to gentamicin (32.4%). *E. coli* and *Klebsiella* species isolates from urine were between 74 and 100% susceptible to meropenam, ceftriaxone, ciprofloxacin, ceftazidime (Msaki *et al.*).<sup>7</sup>

UTIs are more common in children with children suffering from sickle cell anemia. Routine screening in those children is, therefore, recommended during febrile illness (Mava *et al.*).<sup>8</sup>

Children are more susceptible for infection. Low bacterial counts, absence of pyuria, or finding a sterile pyuria should not be disregarded (Peard and Maskell).<sup>9</sup>

Febrile UTI is the most common serious bacterial infection in childhood. But, the most appropriate evaluation of children with this condition is still unclear (Buonsenso and Cataldi).<sup>10</sup>

Higher virulence isolates are more likely to cause febrile UTI and to affect children with primary vesicoureteric reflux with no underlying etiology (Storm *et al.*).<sup>11</sup>

## Aims and Objectives

The primary aim of this study was to study the prevalence of UTI in febrile children below 5 years of age and secondarily, the study aimed to determine the spectrum of bacteria causing UTI in children and also to determine the anti-biogram of the bacterial isolates.

## MATERIALS AND METHODS

### Sample Size-100

The study was approved by the Human Ethical Committee of the institution.

The study was conducted at Father Muller Medical college hospital for 3 months. Specimen collected was midstream urine in a sterile container. And the specimens were processed in the microbiology laboratory. The detail information of the patients like name, age, temperature, etc. was extracted in a questionnaire.

All cases of febrile children below 5 years, urine culture, was done by semi-quantitative technique on blood agar, McConkey's agar and the cysteine lactose electrolyte deficient agar (CLED) media and quantitative unspun wet mount microscopy done to detect pyuria (>1 pus cell/7 high-power fields of well-mixed uncentrifuged urine samples),<sup>12</sup> bacteriuria, hematuria or candiduria.

1 µml urine was cultured using a calibrated bacteriological loop on blood agar, McConkey's agar and CLED media, and colonies was counted after overnight incubation at 37°C.<sup>13</sup> Number of colonies obtained was multiplied by 1000 to obtain the colony forming units (CFU)/ml for boys and girls, 10<sup>4</sup> and 10<sup>5</sup> CFU/ml of bacterial growth of a single type of bacteria is taken as a threshold (significant bacteriuria), respectively.<sup>12,14</sup> In case of girls with mid-stream urine showing 10<sup>4</sup>-10<sup>5</sup> CFU/ml, a repeat sample was asked for.<sup>13,14</sup>

Isolates was identified by Gram-stain, motility test and routine biochemical reactions. Antibiotics sensitivity was put up by the Kirby Bauer method following the clinical laboratory standards institute guidelines.<sup>14</sup> All *Enterobacteriaceae* and *Acinetobacter* species was tested against first line agents, gentamicin (10 µg), amikacin (30 µg), cefoperazone (75 µg), cefotaxime (30 µg), nitrofurantoin (300 µg), trimethosulphamethoxazole (1.25-23.75 µg), nalidixic acid (30 µg), norfloxacin (10 µg), and ciprofloxacin (5 µg).

*Enterococcus* spp. against amoxicillin (10 µg), vancomycin (30 µg), nitrofurantoin (300 µg), ciprofloxacin (5 µg), and high level amino glycoside resistance gentamicin (HLAR-G, 120 µg).

*Pseudomonas aeruginosa* against amikacin (30 µg), cefoperazone (75 µg), gentamicin (100 µg), ceftazidime (30 µg), and ciprofloxacin (5 µg). Second line antibiotics were tested only for bacteria in those isolates resistant to all first-line antimicrobials or specifically requested by the attending physician.

ATCC 25922, *E. coli* ATCC 35218 and *P. aeruginosa* ATCC 27853 were used as controls. Apart from demographic data, risk factors and underlying illness will be looked for. Symptomatic UTI was defined and further characterized as community acquired or hospital acquired as per centers for disease control case definition.<sup>14</sup>

### Implications

This study will help

1. To determine the prevalence of UTI in febrile children and to treat with appropriate antibiotics
2. To study the antibiotics sensitivity pattern of the urinary isolates in this geographical region.

### Inclusion Criteria

Patients below 5 years of age, whose temperature is more than 37°C are included, and their mid-stream urine samples are collected.

### Exclusion Criteria

Patients who are catheterized are excluded from the study as chances of contamination of the urine samples are more.

## OBSERVATION AND RESULTS

The study was conducted on 100 febrile children, below 5 years of age. Out of which 60 were boys and 40 were girls, catheterized patients were excluded.

Growth was present in 35 patients (>10<sup>5</sup> CFU/ml). i.e., in 21 boys out of 60 boys and 14 girls out of 40 girls taken for the study. The Age and gender wise distribution of microbiological profile given in Table 1.

In the culture *E. coli* was the predominant organism grown, i.e., it was present in 13 (37.14%) patients out of 35 patients. Followed by *Klebsiella* in 7 patients (20%), *Enterococcus* in 5 patients (14.285%), *Staphylococcus aureus* in 4 (11.4287%) patients, *Citrobacter* and *Pseudomonas* in 2 patients each (5.714%), and *Acinetobacter* and *Protens* in 1 patient each (2.857%). One patient who had UTI is found to have vesicoureteric reflux.

### Antibiotics

*E. coli* was the predominant organism grown, cotrimoxazole (36.36%), ciprofloxacin (30%), amikacin (91.6%), gentamicin (77.7%), norfloxacin (45.54%), nitrofurantoin (90.9%), cefotaxime (100%), followed by

cefazolin (60%), amoxycylav, oxacillin, cefuroxime (50%) each.

Sensitivity pattern of *E. coli* to higher antibiotics: Highly sensitive to piperacillin/tazobactam (100%), cefoperazone/sulbactam (100%), imipenem (100%), and meropenam (100%).

Resistance pattern of *E. coli*: The entire *E. coli* bacteria grown was completely resistant to ampicillin (100% resistance).

Six *E. coli* out of 13 *E. coli* (i.e., 46.15%) grown was multidrug resistant, i.e., it was resistant to the penicillin group of antibiotics, quinolone group of antibiotics and a cephalosporin group of antibiotics.

*Klebsiella* was the second most bacteria grown. Its sensitivity pattern for first-line antibiotics is as follows: Amikacin (75%), followed by norfloxacin, ciprofloxacin and ceftriaxone (60%), nitrofurantoin, amoxycylav, and ceftazidime (50%).

Sensitivity pattern of *Klebsiella* to higher antibiotics: Piperacillin/tazobactam (66.66%), cefoperazone/sulbactam (66.66%), imipenem (66.66%), meropenam (66.66%).

Resistance pattern of *Klebsiella*: The entire *Klebsiella* organism grown was completely resistant to ampicillin, cefazolin, and cefuroxime (100% resistance). These could be extended-spectrum beta-lactamases (ESBL) producers. Four *Klebsiella* out of seven *Klebsiella* spp grown was resistant to the penicillin group of antibiotics, quinolone group of antibiotics and cephalosporin group of antibiotics. These are multidrug resistant *Klebsiella*.

## DISCUSSION

The study conducted in Department of Pediatrics, The University of Melbourne, Parkville, Victoria, Australia on 735 cases revealed that the commonest organism causing UTI as *E. coli* (67.4%), and *Klebsiella* (7%), whereas this study also has revealed the most common organism causing UTI as *E. coli* but it is only (37.14%), followed by *Klebsiella* (20%) (Tebruegge et al.).<sup>5</sup>

Co-trimoxazole and nitrofurantoin is the most common used antibiotics in the treatment of UTI in tertiary care hospitals. Our study has revealed that nitrofurantoin is 90.9% sensitive and 50% sensitive to *E. coli* and *Klebsiella* a respectively. However, co-trimoxazole is only 36.36% sensitive to *E. coli*.

In a study conducted in sing health polyclinics Bedok, Singapore there was no significant difference in susceptibility

of common oral antibiotics when tested against the enterobacteriaceae for both male and female patients.

The high prevalence of resistance to ampicillin and co-trimoxazole in seen (97-100%).<sup>1</sup> Even in our study, enterobactericia grown was 100% resistant to ampicillin and 36.36% sensitive to co-trimoxazole.

Normally females are more affected by UTI than in males. However in our study, due the unequal number of subjects included, resulted in equal percentage of patients (35% both males and females) affected by UTI.

## SUMMARY

UTI is common in children, mostly in febrile children. Our study has found that 35% of febrile children below 5 years of age are affected by UTI.

*E. coli* is found to be the most common organism causing UTI in febrile children followed by *Klebsiella*. Organism causing UTI are sensitive to the first-line antibiotics like co-trimoxazole, nitrofurantoin, norfloxacin, gentamicin, amikacin, amoxycylav. Whereas *E. coli* causing UTI in febrile children is completely (100%) resistant to ampicillin and *Klebsiella* causing UTI in febrile children is completely (100%) resistant to ampicillin, cefazolin, and cefuroxime.

## CONCLUSION

Our study revealed that *E. coli* are the most predominant organism grown in the culture, which indicates, most common bacteria causing UTI in the febrile children below 5 years of age is *E. coli* and then followed by *Klebsiella*. The study also indicates that kids between 1 and 2 years are more susceptible for infection, even though other age groups are also affected by UTI to a certain extent.

The presence of congenital abnormality in the lower urinary tract makes the individual more prone for the UTI. e.g.: Vesicoureteric reflux.

Antibiotics: First line antibiotics like co-trimoxazole, gentamicin, norfloxacin and nitrofurantoin are sensitive to *E. coli*. For *Klebsiella* first-line antibiotics like co-trimoxazole, nitrofurantoin, norfloxacin, gentamicin, and amikacin are sensitive. Thus, these drugs can be used in the treatment of an uncomplicated community acquired UTI. However, ampicillin is 100% resistant to the *E. coli*; hence its use should be avoided as much as possible. *Klebsiella* is 100% resistant to ampicillin, cefazolin and cefuroxime.

**Table 1: Age and gender wise distribution of microbiological profile in children**

Age in years	Number of children	Number of children with UTI and growth in the media	Percentage of growth in the media	Male: female
<1	10	2	20	2:0
1-2	19	7	36.84	5:2
2-4	42	17	16.66	9:8
4-5	29	9	31.034	5:4

UTI: Urinary tract infection

*Klebsiella* grown which is resistant to ceftazidime and cefuroxime, could be ESBL producers.

*E. coli* and *Klebsiella* organism which is resistant to the penicillin group of antibiotics, quinolone group of antibiotics and cephalosporins group of antibiotics are multi-drug resistant bacteria. Thus, it is important for a physician to treat the UTI with appropriate antibiotics following culture and sensitivity report.

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# Relationship between Obesity and Periodontitis in 20-50 Year Old Adults of South Canara, India

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## Abstract

**Background:** There is an increase in prevalence of obesity all over the world, including developing countries like India. There are studies showing correlation between obesity and periodontitis, but there are contradictory studies too. The purpose of this study is to delineate the relationship between obesity and periodontitis, in a small representative sample of South Indian population, by eliminating the confounding factor tobacco smoking.

**Objective:** The aim was to evaluate the relationship between obesity and periodontitis in 20-50 years old adults in South Canara District, Karnataka, India.

**Materials and Methods:** A cross-sectional descriptive study was conducted to evaluate the relationship between obesity and periodontitis in 20-50 years old adults. Study population consisted of 148 patients who visited Yenepoya Medical and Dental colleges meeting the inclusion criteria. Of the total sample, 74 patients were obese, and 74 were non-obese. The study sample included the age group of 20-50 years old adults. The criteria used to differentiate obese and non-obese subjects were based on the criteria given by World Health Organization (2000). (i.e., body mass index [BMI]  $\geq 30$  kg are obese). BMI was calculated as body weight in kg/height in meter square. The periodontal status was compared between obese and non-obese persons by community periodontal index and loss of attachment. Informed consent was obtained prior to examination from the subjects. Data were statistically analyzed using SPSS version 18 and Pearson's Chi-square test.

**Results:** In this study, prevalence of periodontal disease was higher in the obese group (59.6%) when compared to the normal group (40.4%). However, the association was not statistically significant. ( $P = 0.063$ ).

**Conclusion:** Prevalence of periodontal disease is higher in the obese group, but there is only a weak association between obesity and periodontitis.

**Keywords:** Body mass index, Obesity, Old adults, Periodontitis

## INTRODUCTION

Obesity is a chronic disease with multifactorial etiology, in which excess body fat has accumulated to the extent that it have an adverse effect on general health and life expectancy and also causes disfigurement of the body.<sup>1</sup> The global obesity epidemic has been described by the World Health Organization (WHO) (2000) as one of the most escalating, yet most neglected, public health problems that astounds both more-and less-developed

countries. Statistics have already alerted health care workers, as excess body weight is now the sixth important risk factor contributing to disease worldwide.<sup>2</sup> Obesity is a major culprit for a variety of co-morbidities and complications that affect overall health. Hence, it is high time to consider obesity as a major public health problem today.<sup>3</sup> Statistics reveal that two-thirds of adults in the United States today are obese or overweight. In the United States, 28% of men, 34% of women, and nearly 50% of non-hispanic black women are currently obese. What

that is really alarming is the fact that, the distribution of (body mass index [BMI], the weight in kilograms divided by the square of the height in meters) has shifted in a skewed fashion such that the proportion of people with extreme obesity has increased at an especially rapid rate. These trends are not pertaining to a specific group, but have affected all major racial and ethnic groups, all regions of the country, and all socio-economic strata, with the largest increases in obesity occurring among children and minorities.<sup>4</sup> Obesity is a risk factor for several chronic diseases, such as hypertension, type two diabetes, dyslipidemia, and coronary heart disease. Statistics showed that the cost associated with the management of obesity and obesity-related diseases accounts for about 5% of total healthcare expenditures in most industrialized countries. Hence, it has become mandatory to acquire more knowledge on the versatile areas like obese persons and their management, the need for awareness regarding the change in lifestyles across the spectrum of health professionals, including dentists.<sup>3</sup>

In spite of all this, the Third National Family Health Survey-3 has reported that there is an increasing tendency of obesity in Indian population. Cross sectional studies suggest that the obesity is also associated with oral diseases,<sup>2</sup> but its severity and extent still not clearly defined. On accordance with the advent of newer diagnostic methods recent studies have suggested that obesity is associated with oral diseases, particularly the periodontitis. Periodontitis is an inflammatory disease of the supporting tissues of the teeth. It can be caused by specific microorganism or group of a specific microorganism, resulting in progressive destruction of the periodontal ligament and alveolar bone. Cardinal signs of periodontal destruction are pocket formation, recession, or both. Fat tissue as we consider, is not merely a passive triglyceride reservoir of the body, but also produces a vast amount of inflammatory cytokines and hormones, that has a devastating effect on the periodontium. There are enough evidences for the fact that inflammatory diseases like periodontitis induce the production of pro-inflammatory cytokines such as tumor necrosis factor alpha (TNF- $\alpha$ ), interleukin (IL-1), and IL-6.<sup>3</sup> TNF- $\alpha$  plays a crucial role in the development of periodontitis. An enhanced level of TNF- $\alpha$  is reported in gingival-crevicular-fluid (GCF) in patients with periodontitis.<sup>5</sup> These observations suggest that there can be considerable correlation in the incidence of obesity, periodontitis, and associated chronic diseases. All these can be complementary, i.e., one predispose to the other, which makes the measurement of correlation cumbersome. However, present studies are insufficient to conclude whether such associations are causal.<sup>3</sup> Hence the current study was conducted with an objective to evaluate the relationship between obesity and periodontitis in 20-50 years old adults in South Canara, India.

## MATERIALS AND METHODS

A cross-sectional descriptive study was conducted for a period extending from May-November 2013. Sample size had been taken on the basis of allowable error of (L) of 6%. Study sample consisted of 148 patients attended Yenepoya medical and dental college's outpatient department (OPD) who met the inclusion criteria. Of the total sample, 74 patients were obese, and 74 were non-obese. Ethical clearance was obtained from Institution Ethics Committee, Yenepoya University (YUEC118/1/6/2013). The inclusion criterion for the study was as follows: Dentate persons with minimum six or more teeth including both upper and lower dental arches between the age group of 20-50 years, who were non-smokers (who had quit smoking cigarettes after smoking for <10 years, those who had no history of smoking). Obese and non-obese persons without any systemic diseases. Patients who have not received periodontal treatment or antibiotics for at least 3 months prior to study. Individuals who provide consent to participate in the study. Chronic use of anti-inflammatory drugs and premedication 3 months prior to the study, pregnancy were categorized as exclusion criteria's.

The criteria used to differentiate obese and non-obese subjects based on the criteria given by WHO 2000 (i.e., BMI  $\geq 30$  kg are Obese).<sup>6</sup> BMI was calculated as body weight in kg/height in meter square. The periodontal status was compared between obese and non-obese persons by community periodontal index and loss of attachment. Variables relating to the measurement of periodontal supporting tissues include attachment loss, probing depth and furcation involvement. Periodontitis group involved dentate individuals having, one or more teeth with  $>3$  mm probing depth or one or more posterior teeth with Grade I furcation involvement.<sup>7</sup> An examination was carried out by a single examiner, with the assistance of a recorder. Informed consent was obtained prior to examination from the subjects. The BMI of the study population was calculated and conducted two-sample independent T-test. Data was statistically analyzed using Statistical Package for the Social Sciences version 18.0 (Inc, Chicago, USA) and Pearson's Chi-square test was used to determine the association of BMI with periodontitis.

## RESULTS

The present study comprised a total of 148 subjects including 114 males and 34 females. When we consider the prevalence of the periodontal loss in study population, of the total 148 subjects, 91 subjects were free of periodontal disease and 57 subjects had periodontitis (Table 1). Of the total 114 males examined, only 72 males were free

of periodontal disease and 42 males had periodontal disease. Of the 34 females, only 19 females were free of periodontal disease and 15 females had periodontal disease. In the present study prevalence of the periodontal loss was higher in males (73.7%) when compared to females (26.3%) (Table 2). The BMI of the study population was calculated and conducted two-sample independent T-test. There is a statistically significant difference in mean BMI between two groups. ( $P < 0.001$ ) (Table 3).

Comparing the relationship between obesity and periodontitis in the study population, in the non-obese group (control) out of 74 subjects, 51 subjects (56%) were free of periodontal disease and 23 subjects (40.4%) had periodontal disease. In the obese group (case) out of 74 subjects, 40 subjects (44%) were free of periodontal disease and 34 subjects (59.6%) had periodontal disease (Table 4).

In this study, prevalence of periodontal disease was higher in the obese group (59.6%) when compared to the normal group (40.4%). Data was statistically analyzed using Pearson's Chi-square test (test value-3.452). In this study we found that there was no association between study groups (i.e., non-obese group and obese group) and the periodontal loss ( $P = 0.063$ ).

**Table 1: Sex versus periodontal loss-cross tabulation**

Sex	Normal/healthy (%)	Periodontal disease (%)	Total (%)
Male	72 (79.1)	42 (73.7)	114 (77)
Female	19 (20.9)	15 (26.3)	34 (23)
Total	91 (61.5)	57 (38.5)	148 (100)

**Table 2: Prevalence of the periodontal loss in study population**

Subjects	Frequency	Percent
Subject without periodontal disease	91	61.5
Subject with periodontal disease	57	38.5
Total	148	100.0

**Table 3: To assess the BMI of the study population**

Group	N	Mean	Standard deviation
BMI			
Normal	74	23.946	3.2091
Obese	74	31.770	1.8248

BMI: Body mass index

**Table 4: The relationship between obesity and periodontitis in the study population**

Group	Normal/healthy (%)	Periodontal disease (%)	Total
Non-obese	51 (56)	23 (40.4)	74
Obese	40 (44)	34 (59.6)	74
Total	91	57	148

## DISCUSSION

Obesity is a multifactorial disease. There are several possible mechanisms that could explain the relationship between obesity and periodontitis. Adipose tissue, can be considered as an endocrine organ, because it secretes adipokines like TNF- $\alpha$ , IL-6, IL-8, leptin, plasminogen activator inhibitor-1, resistin, and angiotensinogen.<sup>5</sup> Recent researches reported that TNF- $\alpha$ , in adipose tissue, has been shown to cause liver injury in obese patients, and this can predispose to insulin resistance.<sup>8</sup> It has been suggested that the Lipopolysaccharides from periodontal Gram negative bacteria can trigger secretion of TNF- $\alpha$  by adipose tissue which promotes hepatic dyslipidaemia and decreases insulin sensitivity. Production of advanced glycation end products, as a result, of type two diabetes and decreased insulin sensitivity is the main pathogenesis for periodontitis as it triggers inflammatory cytokine production.<sup>3</sup>

Obesity even affects host immunity. Studies conducted in obese, hypertensive rats have showed that they had a higher incidence of periodontitis than normal rats, and have intimal periodontal blood vessel thickening, indicating diminished blood flow. Visceral fat shows increased expression of plasminogen activator inhibitor-1 gene, which is responsible for diminished periodontal blood flow, predisposing to periodontitis and its progression.<sup>8</sup>

In this study prevalence of periodontal disease was higher in the obese group (59.6%) when compared to the normal group (40.4%). This finding is in agreement with the study conducted by Mathur *et al.*,<sup>2</sup> Linden *et al.*<sup>9</sup> In the present study, subjects categorized as obese ( $\geq 30$  kg/m<sup>2</sup>) were observed to have no association with periodontal disease ( $P = 0.063$ ). Our findings are consistent with the study done by Kim *et al.*<sup>10</sup> where he found no association between BMI and periodontitis, but a significant association between abdominal obesity and periodontitis was found. In the present study, waist, circumference was not recorded as this would be embarrassing to the female study population. Ylöstalo *et al.*<sup>11</sup> detected a weak exposure association of BMI with deepened periodontal pocket.

This study utilized the BMI classification as given by WHO to determine obesity.<sup>12</sup> But recent studies are highlighting the need for a different classification for the Asian population's they are more susceptible to obesity-related conditions, where BMI  $\geq 25$  kg/m<sup>2</sup> is considered as obese.<sup>13</sup> The modified classification system suggests that BMI  $< 18.5$  kg/m<sup>2</sup> indicates underweight, 18.5-22.9 kg/m<sup>2</sup> indicates normal weight, 23-24.9 kg/m<sup>2</sup> may be considered as overweight, and  $\geq 25$  kg/m<sup>2</sup> are obese.<sup>14</sup> Because of the lack of evidence and sufficient literature, more studies should be conducted regarding this; it was tempting to

follow the traditional classification. In the present study, prevalence of the periodontal loss was higher in males (73.7%) when compared to females (26.3%). This finding is in accordance with the study conducted by Dalla Vecchia *et al.*<sup>15</sup> The present finding is not in agreement with the study conducted by Mathur *et al.*<sup>2</sup>

Smoking is now considered to be one of the significant risk factor in development and progression of periodontal disease. Smokers have deeper pockets and greater attachment loss compared to non-smokers.<sup>16</sup> Studies have shown that Smokers have approximately 3 times more risk for severe periodontitis than non-smokers and chance of improvement following periodontal therapy is just the half.<sup>17</sup> There are many epidemiological studies suggesting consistently found poorer oral hygiene in tobacco smokers than in non-smokers. There are reports of increased quantities of calculus in smokers. Evidences shows that tobacco smoke and water soluble components of tobacco smoke adversely affect the chemotactic and phagocytic ability of normal polymorphonuclears.<sup>18</sup> There are reports of the increase in GCF volume with the degree of inflammation. The increased volume of GCF shows the presence of marked inflammation in smokers.<sup>19</sup> In this study smokers were excluded hoping that this will delineate the relationship between obesity and periodontitis better.

Considering the limitations of this study, stress, socio-economic status and oral hygiene practices could confound the results. Furthermore, this study should be conducted in a large population to correctly assess the relationship between obesity and periodontitis. Also, the study population was limited to patients coming to the OPD. In the present study, the severity of periodontal disease was not actually examined. The main concern was whether the disease is present or absent.

## CONCLUSION

Within the scope and limitations of this study, the following observations are made: Prevalence of periodontitis was higher in the obese group than normal group. The prevalence of the periodontal loss was more in obese males than in obese females. Future longitudinal studies are needed to confirm these findings and extend them to more diverse populations. In periodontal disease prevention campaigns, it's time to highlight obesity prevention. Discussing the patient's weight in the dental

setting although that is quite embarrassing to some patients should be the prevention strategy what we need to look forth. Also, the dental workforce should concentrate on giving dietary advice, a topic they are more familiar with and confident to deliver.

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# Comparison Between 0.15% Ropivacaine Plus Fentanyl 2 µg/ml and 0.10% Levobupivacaine Plus Fentanyl 2 µg/ml for Labour Epidural Analgesia: A Double-Blind Randomized Study

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## Abstract

**Background:** The purpose of this prospective study was to assess whether a combination of 0.10% levobupivacaine plus 2 µg/ml fentanyl had the same effects as 0.15% ropivacaine plus 2 µg/ml fentanyl on the mode of delivery and other obstetric outcomes when used for labour epidural analgesia.

**Methods:** This double-blind, randomized, prospective study was performed in 100 parturients who requested epidural analgesia. After a lumbar epidural catheter had been placed, patients received either 0.10% levobupivacaine plus 2 µg/ml fentanyl or 0.15% ropivacaine plus 2 µg/ml fentanyl followed by a continuous infusion. Additional boluses were used for inadequate levels of analgesia. Visual analog pain scores, motor block, level of sensory block, supplementary boluses and main characteristics of labour were recorded.

**Results:** There were no significant differences in the mode of delivery, duration of labour, or neonatal outcome between the two groups. In the levobupivacaine group, the parturients required top-up boluses of local anesthetics more frequently ( $1.4 \pm 1.6$  vs.  $0.9 \pm 1.3$ ,  $P < 0.0001$ ), and the incidence of temporary maternal fever (12 vs. 7,  $P = 0.024$ ) were higher. However, the amount of local anesthetic administered during labour was lower ( $52 \pm 10$  mg vs.  $59 \pm 10$  mg,  $P < 0.0001$ ) than for the ropivacaine group.

**Conclusions:** About 0.10% levobupivacaine was as effective as 0.15% ropivacaine, when both were used with 2 µg/ml fentanyl for labour epidural analgesia

**Keywords:** Fentanyl, Labour analgesia, Levobupivacaine, Obstetric outcome, Ropivacaine

## INTRODUCTION

Epidural anesthesia is an effective means of providing analgesia during labour. Although epidural bupivacaine is highly effective in providing pain relief, its use is limited because of side effects including motor blockade and cardiovascular toxicity.<sup>1</sup> Dilute solutions of epidural bupivacaine combined with opioids have been used to minimize the unwanted local anesthetic effect of motor block. Levobupivacaine and ropivacaine are new local anesthetics that have effects similar to bupivacaine. They

are believed to be less toxic to the central nervous system and cardiovascular system. They have also been reported to cause less motor blockade.<sup>2-4</sup>

However, two recent studies have shown that, about analgesic effect, ropivacaine is 60% as potent as bupivacaine when used for epidural pain relief in labour.<sup>5,6</sup> Therefore, previous comparisons of the incidence of motor block between these two anesthetics were carried out using relatively more bupivacaine than the ropivacaine when the potency difference is considered.

The aim of this study was to compare motor block provided by equianalgesic concentrations of ropivacaine (0.15%) and levobupivacaine (0.10%) combined with 2 µg/ml fentanyl for analgesia during labour.

## METHODS

The protocol was approved by the local Ethics Committee and written informed consent was obtained from each patient. One hundred parturients classified as American Society of Anesthesiologists physical Status I or II who requested epidural analgesia were enrolled in the study. An uncomplicated course of pregnancy and normal fetal heart rate before randomization were necessary inclusion criteria. Participants were para 0 or 1,  $18 \pm 40$  year old, with a singleton pregnancy of more than 37 weeks and vertex presentation. All women were in active labour with cervical dilatation of  $3 \pm 7$  cm and a visual analog pain score  $>30$  mm. None was receiving parenteral opioids before epidural placement.

Patients were placed in the flexed sitting position and were monitored with a non-invasive blood pressure cuff, pulse oximetry and cardiotocography. The epidural space was identified using the loss of resistance technique at the L2-L3 or L3-L4 level, and a multiport epidural catheter was advanced 4 cm into the epidural space. Afterwards, a test dose was performed using 0.25% bupivacaine with adrenaline 1 in 2 lakh solution 3 ml.

Participants were allocated to one of two groups in a double-blind, randomized, prospective study design. Patients were assigned to one of the two treatments using a random number table. The procedure of randomization and the handling of the treatment vials was the responsibility of the pharmacy in our institution. Epidural solutions were prepared with either 0.10% levobupivacaine plus 2 µg/ml fentanyl or 0.15% ropivacaine plus 2 µg/ml fentanyl. The anesthetists performing the procedure and subsequent assessment were blinded to the local anesthetic used. Patients lay on their left side before injection of drugs. According to the patient's height, the initial bolus was 10 ml (height  $<160$  cm), 15 ml (height 160-170 cm) or 20 ml (height  $>170$  cm) and was followed by an infusion of 6-10 ml/h according to the various standard recordings (electrocardiography, automated non-invasive blood pressure, and fetal heart rate monitoring). Epidural analgesia was continued through the second stage of labour. Decisions concerning obstetrical management were made by the attending obstetrician.

Maternal age, height, body weight, presence or absence of spontaneous rupture of membranes at admission,

admission white blood cell (WBC) count, and time interval from admission to initiation of epidural analgesia were recorded as the pre-labour characteristics. The following were recorded as labour characteristics: time interval from admission to delivery, duration of the epidural analgesia, duration of the second stage, the total amount of local anesthetic uses as top-up bolus doses and their frequency of administration, and the parturients complaints after epidural anesthesia (including nausea, vomiting, and fever). The definition of maternal fever for this study was an ear temperature  $>38^{\circ}\text{C}$ . Mode of delivery, Apgar scores of the new born, body weight of the new born, temperature of the new born, whether antibiotics were administered to the parturients during the peripartum period, the presence of postpartum hemorrhage (PPH), and the total amount of local anesthetics were recorded as the labour outcome characteristics.

Data are presented as mean  $\pm$  standard deviation. Differences in categorical variables were analyzed by the Chi-square and test.  $P < 0.05$  was considered as statistically significant.

## RESULTS

Information on the 100 parturients was collected. A sample size of 100 will have the power of 99.6% when detecting differences and the  $\alpha = 0.05$ . Three patients (one in the levobupivacaine group and two in the ropivacaine group) were excluded from data analysis: One patient experienced a failure of analgesia, and the epidural catheter had to be replaced, data collection was incomplete in one patient and one patient was delivered before 30 min. Of these parturients, 48 belonged to the ropivacaine group and 49 to the levobupivacaine group. No differences were observed in the pre-labour characteristics between the two groups (Table 1).

The parturients in the levobupivacaine group required top-up boluses of local anesthetics for adequate pain relief more frequently ( $1.4 \pm 1.6$  vs.  $0.9 \pm 1.3$ ;  $P < 0.0001$ ),

**Table 1: Pre-labour characteristics**

Description	Ropivacaine group (n=48)	Levobupivacaine group (n=49)	P value
Age (years)	28 $\pm$ 4	28 $\pm$ 3	0.363
Height (cm)	162 $\pm$ 5	162 $\pm$ 5	0.097
Weight (kg)	64 $\pm$ 8	63 $\pm$ 9	0.081
Spontaneous rupture of membranes	19	18	0.583
Admission WBC count (1000/ $\mu\text{L}$ )	10.2 $\pm$ 3.2	10.4 $\pm$ 3.1	0.750
Time interval from admission to initiation of epidural analgesia (min)	247 $\pm$ 280	211 $\pm$ 180	0.207

WBC: White blood cell

and the rate of temporary maternal fever during the peripartum period was also higher in this group (12 vs. 7,  $P = 0.024$ ) than in the ropivacaine group. No differences were observed for the time interval from admission to delivery, the duration of epidural analgesia, the duration of the second stage, the total in milligrams of the bolus doses, and frequency of nausea and vomiting (Table 2).

About the labour outcome characteristics, no differences were observed in the mode of delivery, Apgar score of the newborn, new born weight of the newborn, frequency of fever in the newborn, antibiotic administration to parturients during the peripartum period, and the occurrence of PPH. More local anesthetic ( $59 \pm 14$  mg vs.  $52 \pm 10$  mg;  $P < 0.0001$ ) was administered during labour in the ropivacaine group (Table 3).

## DISCUSSION

The results of our study demonstrated that there was no significant difference in the mode of delivery, duration of labour, or neonatal outcome between the two drugs when

**Table 2: Labour characteristics**

Description	Ropivacaine group (n=48)	Levobupivacaine group (n=49)	P value
Time interval from admission to delivery (min)	860±522	810±456	0.270
Duration of epidural analgesia (min)	556±329	510±311	0.609
Duration of second stage (min)	80±56	85.6±1	0.194
Frequency of top up boluses	0.9±1.3	1.4±1.6	<0.0001
Total boluses does (mg)	24±35	18±21	0.084
Frequency of nausea and vomiting	6	4	0.349
Frequency of maternal fever	7	12	0.024

**Table 3: Labour characteristics**

Description	Ropivacaine group (n=48)	Levobupivacaine group (n=49)	P value
Vaginal delivery	34	37	0.269
Instrumental delivery	9	6	
Cesarean delivery	5	6	
Apgar score of new born <8 at 1 min	2	2	>0.99
New born weight (g)	3091±371	3107±345	0.501
Frequency of new born fever	7	7	>0.99
Antibiotic use	24	22	0.615
Total use of local anesthetic (mg)	59±14	52±10	<0.0001
PPH	1	1	>0.99

PPH: Postpartum hemorrhage

used with the above regimens. The use of levobupivacaine in labour analgesia has been previously compared with that of ropivacaine at similar or different concentrations.<sup>7-10</sup> Beilin *et al.* demonstrated that there was no significant difference in the total dose of local anesthetic administered per hour or the number of top-up doses required per hour during labour when 0.15% ropivacaine or 0.10% levobupivacaine were used with 2 µg/ml fentanyl.<sup>9</sup> Further, Purdie and McGrady found that 0.1% ropivacaine or 0.1% levobupivacaine, both administered with 2 µg/ml fentanyl, necessitated the administration of the same number of rescue top-up doses, and hence, seemed pharmacologically equipotent.<sup>7</sup> Ati  zar *et al.* found that there were no significant differences in the total dose of local anesthetic and the number of rescue boluses when 0.2% ropivacaine or 0.125% levobupivacaine was used with 0.0001% fentanyl.<sup>10</sup> In contrast, Smet *et al.* in their article compared 0.165% ropivacaine and 0.125% levobupivacaine, both administered with 0.0001% sufentanil, for patient-controlled epidural analgesia for 24 h after orthopedic surgery. They found that even at a 25% weaker concentration, a lower amount of levobupivacaine was required, which may be explained by a difference in potency of or the duration of action of the levobupivacaine.<sup>11</sup> In this study, even if our data showed that the total doses of local anesthetic were significantly higher in the 0.15% ropivacaine group than in the 0.10% levobupivacaine group, it is difficult to evaluate the relative potency of the two drugs in this type of a retrospective study. Furthermore, the inclusion of fentanyl might also influence the quality of analgesia.<sup>12</sup> The more frequent use of a top-up bolus was noted with levobupivacaine and, therefore, daily practice can be improved by increasing the top-up bolus dose, which will then decrease frequency of use when levobupivacaine is used.

The incidence of fever in nulliparous women continuously receiving analgesics varies from 14.5% to 33% and increases with the duration of epidural use.<sup>13-15</sup> The rise in temperature is often temporary, and the temperature may normalize at or soon after delivery.<sup>16</sup> In some parturients, the fever is caused by infection, usually chorioamnionitis, but in most cases, the origin of the fever is unknown. Intermittent epidural injections as against continuous analgesic infusion appear to prevent intrapartum fever during the first 4 h of labour analgesia.<sup>17</sup> Several theories have been proposed as to the mechanism of epidural fever, and they largely emphasize the changes in maternal thermoregulation. Goetzl *et al.* found that epidural fever is associated with an elevated maternal serum interleukin-6 level, which supports an inflammatory basis for epidural fever.<sup>18</sup>

Based on our results, there were no significant differences in the incidence of spontaneous rupture of membranes

at admission, admission WBC count, and the duration of epidural analgesia between the two groups. Nonetheless, the rate of temporary maternal fever was higher in levobupivacaine group ( $n = 12$ ) than in the ropivacaine group ( $n = 7$ ) ( $P = 0.024$ ). All the 19 fever parturients had a normal temperature before epidural analgesia. The C-reactive protein (CRP) and the WBC counts were checked in the parturients that fever was suspected to pinpoint any possible infection. In the Ropivacaine group, there were 5 out of 7 (72%) parturients who had an elevated CRP value or WBC count. In the Levobupivacaine group, there were 7 of 12 (63%) parturients who had an elevated CRP value or WBC count. The temperatures of these mothers recovered to the normal range within 24 h after delivery in 17 of 19 parturients. Only two participants showed persistent fever for >24 h after delivery, and both belonged to the levobupivacaine group. One parturient had chorioamnionitis, while the other had a fever of unknown origin. We do not know the exact mechanisms by which the levobupivacaine group seemed to cause a higher percentage of maternal fever. Even so, although the rates of maternal fever between the groups were different, no significant differences were observed in antibiotic use and neonatal outcome. No difference between the two drugs with respect to maternal fever could be found in any recent publications and, therefore, more research is required in this area.<sup>7-10</sup>

## CONCLUSION

On the basis of the currently available data, it can be concluded that 0.10% levobupivacaine is as effective as 0.15% ropivacaine when both are used with 2 µg/ml fentanyl during labour epidural analgesia.

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# Clinical Study and Management of Inguinal Hernias by Lichtenstein Repair

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## Abstract

**Introduction:** Inguinal hernia is the most common condition requiring major surgery among abdominal wall hernia. Despite the frequency of surgical repair, perfect results continue to elude surgeons, and the rate of surgical failure (recurrence) is humbling.

**Purpose:** This study was carried out to evaluate. Early post-operative pain experienced by the patient (1) Development of post-operative complication, (2) The recurrence rate by this procedure, (3) The chronic pain experienced by the patient due to mesh.

**Materials and Methods:** This clinical study of Lichtensteins open tension free hemioplasty was conducted on the patients admitted with the diagnosis of both primary and recurrent inguinal hernias in BLDE University Shri B.M.Patil Medical College, Hospital and Research Center during the year January 2011 to January 2014. All the cases were operated under spinal anesthesia using 7.6 cm × 15 cm polypropylene mesh. These patients were followed-up for early and late complications.

**Results:** In our study, patients aged ranging from 20 to 75 years, more than 48% was over 51 years old. The greatest incidence was in the 51-60 years of age group (26%). In 150 patients 14% (21 cases) had benign enlargement of the prostate, 40% (60 cases) had a habit of smoking. About 10% of patients (15 cases) had chronic obstructive pulmonary disease, 2% of patients (3 cases) had urethral stricture and 6% of patients (9 cases) had diabetes mellitus (DM) alone as their associated factors. Indirect inguinal hernia constituted 68% and direct hernia constituted 28%, and recurrent hernias was present in 4%. Pain was occurred in a mild degree for 44% (66 cases) of patients. Moderate degree 56% (84 cases) and none of the patient had severe pain.

**Conclusion:** At present, Lichtenstein technique can be considered as the gold standard of groin hernia repair. As it has very low recurrence rate and well tolerated by patients.

**Keywords:** Inguinal hernia, Lichtenstein repair, Pain

## INTRODUCTION

Inguinal hernia is the most common condition requiring major surgery among abdominal wall hernia. Despite the frequency of surgical repair, perfect results continue to elude surgeons, and the rate of surgical failure (recurrence) is humbling.

Since the 19<sup>th</sup> century, when the modern techniques for repair of growing hernia were first described, recurrence was a problem. All repairs namely Bassini's, Halstead, Shouldice, MacVay repairs regardless of modification, have shared a common disadvantage, suture line tension. This

tension is the cause of eventual suture or tissue disruption and the prime etiologic factor in hernia recurrence. Most of these repairs include suturing of the structures under tension, which are normally not in opposition.<sup>1</sup>

The Lichtenstein tension free mesh repair has opened a new era in groin hernia repair. Without the risk of serious morbidity, it can be readily carried out on patients previously considered unsuitable for hernia repair. Fears of complication related to mesh implantation have proved to be without foundation. Lichtenstein recognized that suture line tension was at the heart of failed hernia repairs and that solving this problem would largely eliminate recurrences.<sup>2</sup>



### Aims and Objectives

This clinical study of Lichtenstein open tension free hemioplasty was done to evaluate.

Early post-operative pain experienced by the patient.

Development of post-operative complication such as wound seroma, wound hematoma, wound infection, testicular swelling.

To study the recurrence rate by this procedure.

To study the chronic pain experienced by the patient due to mesh implantation.

## MATERIALS AND METHODS

This clinical study of Lichtenstein's open tension free hemioplasty was conducted from the patients admitted with the diagnosis of both primary and recurrent inguinal hernias in BLDE University Shri B.M.Patil Medical College, Hospital and Research Centre during the year January 2011 to January 2014.

Patients were included in the study based on the inclusion and exclusion criteria as mentioned below.

### Inclusion Criteria

- Age of the patient 20-75 years.
- Patients diagnosed as both primary and recurrent inguinal hernias.
- Patients who gave consent for the procedure.

### Exclusion Criteria

- Patients younger than 20 years and older than 75 years of age
- Patients with strangulated hernias
- Presence of skin infections
- Patients who refused for the procedure.

Patients who fulfilled the above criteria were interviewed, and clinical examination was done based on a prepared questionnaire. Diagnosis was done mainly based on clinical findings, and only those investigations were done which were relevant to obtain a fitness for surgery. This included random blood sugar, blood urea, serum creatinine, electrocardiography hemoglobin percentage and routine urine analysis for sugar, albumin and microscopy chest X-ray and ultrasound abdomen. If any patient was found to have any medical contraindication for surgery, he was first treated for these medical problems and then re-evaluated for surgery.

All the cases were carried out under spinal anesthesia. These patients were subjected to Lichtensteins open tension free hernioplasty using 7.6 cm × 15 cm polypropylene mesh

made. These patients were followed-up by Visual analogue scale, wound hematoma, wound seroma, wound infection and testicular swelling. Late complications like chronic inguinal pain, testicular atrophy and recurrence of hernia.

Patients were assessed for the severity of pain on day 2 and day 5 after surgery by visual analogue scale, which consists of a 10 cm line anchored at one end by a label as no pain and at the other end by a label such as a severe pain. Scoring is accomplished by having the patient mark the line to indicate pain intensity and the line is measured to the mark on 1-10 scale. We translated this for documentation as 1-3 mild pain, 4-7 moderate pain and 8-10 severe pain. 12 patients were called to the outpatient department and follow-up was done for complications like inguinodynia, testicular atrophy and recurrence.

## RESULTS

In our study, patients ranged in age from 20 to 75 years, more than 48% was over 51-years-old. The greatest incidence was in the 51-60 years of age group (26%). Patients between 21-30 and 41-50 years constituted (Table 1).

Among the patients studied 42% (21 cases) came to the hospital by 5 months after appearance of swelling. 4% (2 cases) came by 11 months. 42% came by 5 years. 8% came by 10 years, and 4% took 11 years (Table 2, Graph 1).

Among the 150 patients studied 14% (21 cases) had benign enlargement of the prostate (BEP), 40% (60 cases) had a habit of smoking. About 10% of patients (15 cases) had chronic obstructive pulmonary disease, 2% of patients (3 cases) had urethral stricture and 6% of patients (9 cases) had DM alone. In 2% of patients (3 cases) had DM associated with

**Table 1: Age-wise distribution**

Age (years)	Number of cases	Percentage
21-30	33	22
31-40	12	8
41-50	33	22
51-60	39	26
61-70	24	16
71-80	9	6
Total	150	100

**Table 2: Duration of symptoms**

Duration	Number of cases	Percentage
0-5 months	63	42
6-11 months	6	4
1-5 years	63	42
6-10 years	12	8
11+ years	6	4
Total	150	100

hypertension (HT), 2% had DM, HT with ischemic heart disease (IHD). 2% of patients (3 cases) had HT with bronchial asthma (br. asthma). 2% of patients (lease) had HT with IHD. 2% of patients (lease) had tuberculosis. 2% of patient had br. asthma. 2% of patients had chronic bronchitis and 2% had br. asthma with BEP as their associated factors (Table 3).

In 150 cases indirect inguinal hernia constituted 68% and direct hernia constituted 28% and recurrent hernias was present in 4% (Table 4, Graph 2).

Pain was occurred in a mild degree for 44% (66 cases) of patients. Moderate degree 56% (84 cases) and none of the patients had severe pain (Table 5, Graph 3).

Among the 150 patients studied 2% (3 case) developed seroma, which resolved after aspiration. 4% (6 cases) developed infection, which was treated by drainage and antibiotics. None of the patients required mesh removal and none of the patients developed testicular swelling or hematoma (Table 6, Graph 4).

**Table 3: Associated factors**

	Number of cases	Percentage
BEP	21	14
Br. Asthma with BEP	3	2
Br. Asthma	3	2
Br. Asthma/HT	3	2
Chr. Bronchitis	3	2
COPD	15	10
DM	9	6
DM/HT	3	2
DM/HT with CHD	3	2
HT/IHD	3	2
Smoking	60	40
TB	3	2
Urethral stricture	3	2
No associated factor	66	44
Total	150	100

Br. asthma: Bronchial asthma, BEP: Benign enlargement of the prostate, Chr. bronchitis: Chronic bronchitis, HT: Hypertension, IHD: Ischemic heart disease, DM: Diabetes mellitus, TB: Tuberculosis, CHD: Coronary heart disease, COPD: Chronic obstructive pulmonary disease

**Table 4: Type of inguinal hernia**

Diagnosis	Right side	Left side	Number	Percentage
Direct inguinal hernia	18	24	42	28
Indirect inguinal hernia	66	36	102	68
Recurrent inguinal hernia	3	3	6	4
Total			150	100

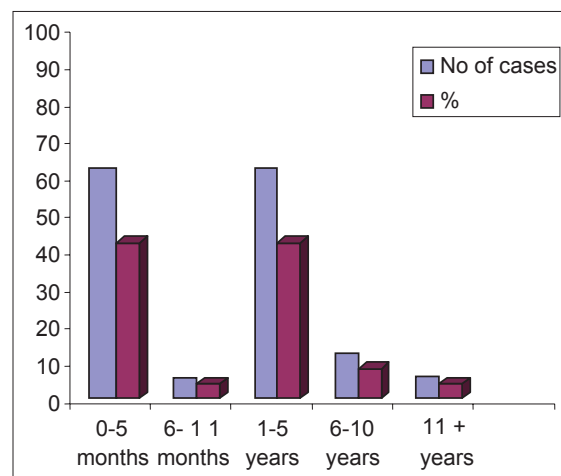
**Table 5: Severity of early post-operative pain**

Pain	Number of cases	Percentage
Mild	66	44
Moderate	84	56
Total	150	100

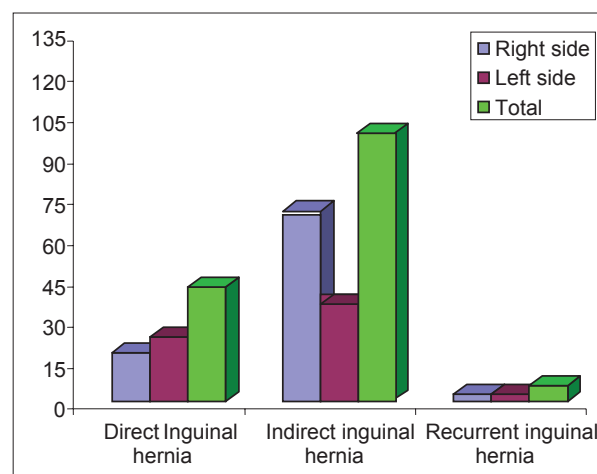
Among the 68% of patients which were followed-up for 6 months to 1 year 1 patient (2%) had recurrence, and 6 patients (4%) had mild pain in the groin (Table 7, Graph 5).

## DISCUSSION

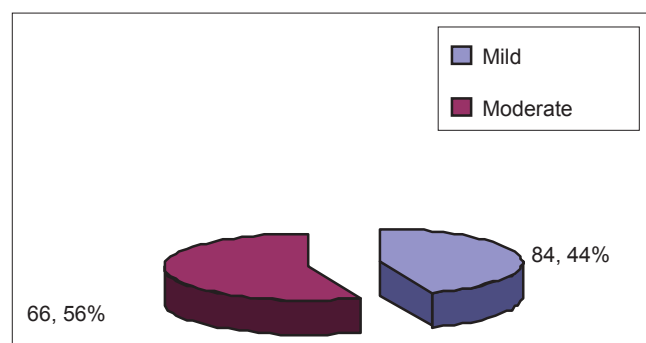
Patients want their period of convalescence and rehabilitation to be uncomplicated in both short and



**Graph 1: Duration of symptoms**



**Graph 2: Type of inguinal hernia**



**Graph 3: Severity of early post operative pain**

long-term outcome so as return to their normal daily activities. As a surgeon, we want techniques with short learning curves, but we still want to attain results comparable to the specialist hernia surgeons.<sup>1</sup>

There is now vast world wide experience with open mesh hernioplasty and there seems little doubt that this approach now appears to be the gold standard when managing inguinal hernias.<sup>2</sup>

The present study is small and randomized and follow-up is limited for 6 months to 1 year. This is considered limitation for my study (Table 8).

Results from Hernias centers are certainly impressive, with recurrence rates of 0.5% or less. My study showed a

**Table 6: Complications**

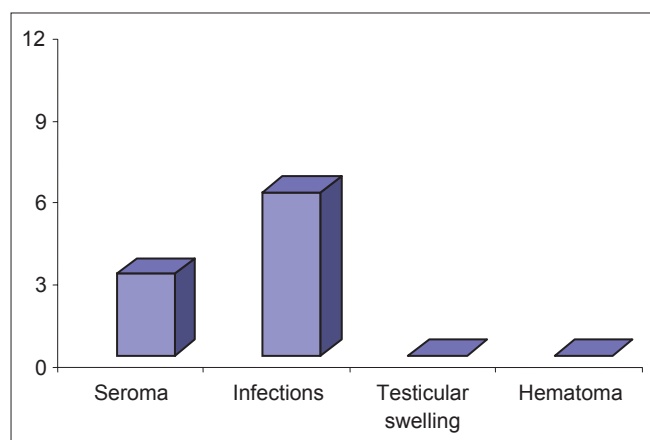
Complications	Number of cases	Percentage
Seroma	3	2
Infections	6	4
Testicular swelling	-	-
Hematoma	-	-

**Table 7: Follow-up**

	Number of cases	Percentage
Follow-up for >6 months	102	68
Last follow-up	48	32
Recurrence	1	0.6
Chronic pain	6	4

**Table 8: Comparative study followup and recurrence**

	Follow-up	Recurrence rate (%)
Lichtenstein <i>et al.</i>	10 years	0.1
Kurzer <i>et al.</i> <sup>2</sup>	10 years	0.1
European Union Trialists	Variable	0.8
Bay-Nielsen <i>et al.</i>	Uncertain	1.3
Present study	1 years	0.6



**Graph 4: Follow up and recurrence cases**

recurrence rate of 0.6%, which occurred in a 75-year-old man after 2 months of surgery, which was small in size and no further repair was attempted. The percentage of recurrence is more compared to other studies. Pain, as we all know, is difficult to measure objectively chronic groin pain (inguinodynia) has until recently been poorly studied by surgeon and considered to be an uncommon complication of hernia repair. Recent prospective and population-based studies, however, have suggested otherwise with the exception of reports coming from centers of expertise, a third or patients studied seen to have some degree of pain 12 or more months often inguinal hernioplasty (Table 9).<sup>3</sup>

In the present study, 6 patients complained of aching sensation in the groin which was mild. Pain did not hinder the day to day activities of the patients. Patients did not need analgesics for pain compared with other studies the percentage of pain is higher.

### Post-operative Infection

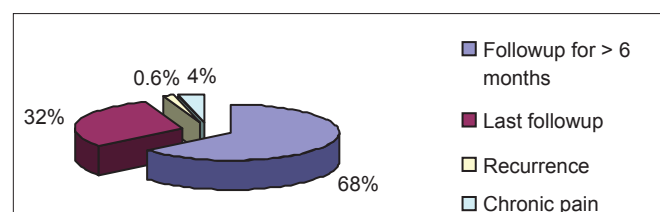
The scenario of the truly infected mesh with or without draining sinuses is one that both surgeon and patients alike dread. The use of mesh is thought by most surgeons to increase wound infection rates, but was largely been supported only by testimony.<sup>4,5</sup>

Mann's review suggested that the increasing numbers of mesh hemioplasties might lead to increasing number of chronic, deep-seated mesh infection, but conceded that reports of this problem were indeed rare. In a recent study from Scotland, however, 12-20 suspected cases of the chronic groin sepsis after mesh hernioplasty were traced. Furthermore, they estimated that the incidence of the chronic groin sepsis following mesh hernioplasty may be approximately 1 in every 1000 (Table 10).<sup>6</sup>

In our study, 6 cases were infected which occurred 1 week after repair and responded to drainage of pus

**Table 9: Comparative study followup percentage**

	Follow-up	Percentage
Lichtenstein <i>et al.</i>	>5 years	2
Kurzer <i>et al.</i> <sup>3</sup>	10 years	1
European Union Trialists	Variable	5
Present study	6 months	6



**Graph 5: Comparative study follow up percentage**

**Table 10: Infection rate in different study**

	Percentage
Lichtenstein <i>et al.</i>	0
Kurzer <i>et al.</i>	1.3
Shulman <i>et al.</i> <sup>7</sup>	0.5
Present study	4

with antibiotic treatment. Patients did not have chronic sinus formation, which needed mesh removal. Compared with other studies percentage is high. Is chronic mesh sepsis really a big problem? The literature is devoid of such reports, whether mesh associated infection are more severe is still an unanswered question in need of objective clinical studies.<sup>8</sup>

## CONCLUSION

The Lichtenstein tension free mesh repair is a straightforward technique to learn without the need for complex instrumentation, overall tests costs can be kept to a minimum without compromising the safety or the

long-term success of the procedure. I conclude the lower age limit of Lichtenstein tension free mesh repair be done to patients more than 20 years of age group. Above all, it has very low recurrence rates and at present it can be considered as the gold standard of groin hernia repair.

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# Management of Infected Non-Unions of Long Bones Using Antibiotic Impregnated Nails

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## Abstract

**Background:** The use of peri-operative antimicrobial prophylaxis and laminar airflow operating rooms has reduced incidence of implant associated infections. However, cases are still commonly encountered in developing countries. Most of the non-unions associated with infected implants usually found resistant to conventional methods of management.

**Aims:** The objective was to evaluate the effectiveness of antibiotic impregnated nails in management of infected non-unions of tibia and femur with bone loss <4 cm.

**Materials and Methods:** This was a prospective study of 18 cases with infected non-unions of femur and tibia, which were enrolled for the study. 14 cases who met all criteria were managed using anti-biotic impregnated nail and were followed-up for an average period of 1.2 years with encouraging results. Under suitable anesthesia, the infected fracture site was exposed and thorough debridement done. Implant was replaced by vancomycin impregnated cement Kuntscher-nail (K-nail)/V-nail following adequate reaming. Culture sensitivity was done at weekly intervals, to identify the pathogen and sensitive antimicrobial agent.

**Results:** All the patients except one, culture revealed no growth and discharge disappeared at the end of 6 weeks. Implant removed after interval of 6-12 weeks depending on the status of infection and callus.

**Conclusions:** Management of Infected non-unions using anti-biotic impregnated K-nail is simple and very effective method which allows infection control, promotes bone union. This simple procedure is encouraging, cost effective and less cumbersome.

**Keywords:** Antibiotic cement nails, Infected non-unions, Vancomycin

## INTRODUCTION

Operative environment underwent a revolution in 21<sup>st</sup> century leading to a drastic decrease in infection rates. However with the increasing number of road traffic accidents and increasing use of orthopedic devices on average 5% of orthopedic devices get infected with added consequences.<sup>1</sup> Infected non-unions of long bones are a disaster both for the surgeon and patient and its management is a challenging task. Traditionally, infected non-unions are managed by staged protocol consisting of stage of infection control, followed by procedures to achieve bony union. Antibiotic beads, long-term antibiotic therapy, repeated debridements have been used to control infection. Stabilizations of fracture with internal and external fixation devices were used to achieve bony union.<sup>2,3</sup> This method of management requires long-term hospital stay with associated social and economic problems. Here we present a novel method of management of infected

non-union of long bones using antibiotic cement nails which aim to control infection by providing high doses of local antibiotics and stabilize fracture at single setting with minimal complications.<sup>4</sup> The aim of our study is to evaluate the effectiveness of antibiotic nails in management of infected non-unions of long bones in terms of infection control and bony union.

## MATERIALS AND METHODS

This prospective study conducted from July 2012 to May 2014. Inclusion criteria were infected non-unions of tibia and femur with no evidence of union by 6-8 months and with bone loss of <4 cm. Patients with radiologically visible or intraoperative finding of gap non-union of more than 4 cm, patients with multiple medical co-morbidities and those with hypersensitivity to vancomycin were excluded from the study.



Out of eighteen patients (Table 1) who presented to our outdoor with infected non-unions of tibia and femur, 14 cases met all the criteria and were enrolled for the study. All patients were thoroughly investigated and evaluated by clinical and radiological means. Out of 14 cases there were 13 male and one female patient. Age group of patients ranged from 18 to 46 years with a mean age of 33 years. Six cases had sustained closed fractures, three each of Grade 2 and 3A fractures and rest two had sustained Grade 3B fractures. Mean duration from injury to presentation was 7 months (6-10 months). Out of 14 cases 9 had femoral non-unions and rest had tibia non-unions. Out of nine femur cases five had intramedullary interlocking nail (ILN) and 4 had Kuntscher-nails (K-Nails). And out of five tibia non-unions three had intramedullary nail, and two had initial AO fixators (3 months), followed by plaster cast treatment. *Staphylococcus aureus* was isolated in 10 cases, one each of *Proteus* and *Pseudomonas aeruginosa* were isolated. Rest 2 cases showed polymicrobial picture. All patients had undergone one or more procedures (debridement, screw removal) before presentation.

### Procedure

All patients who were to undergo antibiotic cement nailing were thoroughly evaluated. Their blood parameters were stabilized, and they were put on culture sensitive antibiotic therapy preoperatively. Under suitable anesthesia part prepared and draped. Non-union site was exposed utilizing old surgical scars, taking care not to undermine skin edges where soft tissue coverage was minimal (shin of tibia). Implant removal done first. The removed implant along with per operative samples was sent for culture and sensitivity. Non-union site was thoroughly debrided excising all the dead and devitalized bone and soft tissues till freshly bleeding bone edges visualized (papkira sign) (Figure 1). After thorough debridement, the bone gap created was determined. Those cases with bone loss more than 4 cm underwent stabilization of the fracture with limb reconstruction system (LRS) or Ilizarov.

Patients with bone loss <4 cm underwent thorough reaming of the intramedullary canal to a width 2-3 mm more than initial nail diameter. Later continuous gravity assisted ingress and egress intramedullary lavage performed with normal saline (4-5 L) till all the granulation tissue was cleared from medulla or clear fluid comes out.

### Antibiotic Cement Nail Preparation

Performed manually on a separate trolley taking all the aseptic measures (Figure 2). Before nail preparation done the surgeon and assistant for nail preparation changed the gown and gloves for performing clean portion of the surgery. K-Nail (cases with Femur Non-union) or V-Nail (for tibia No-unions) of appropriate diameter 2-3 mm thinner than last reamer width was chosen. Nail of 6-8 mm diameter were chosen in most cases. The polymethylmethacrylate bone cement of 40 g mixed with 4 g of vancomycin powder. Monomer solution added to this powder and mixing done till the material acquires viscous consistency. Now manually the antibiotic cement applied uniformly over the nail leaving eye open and cement allowed to set. Diameter of the nail assessed and excess cement trimmed off by passing nail through nail width measurer. Remaining antibiotic cement was discarded. After nail completely sets it was passed into the intramedullary canal in a retrograde fashion for femur and in ante grade fashion for tibia. Hemostasis secured and closure was done in layers over a suction drain.

### Post-operative Protocol

All patients were put on culture sensitive parenteral antibiotics for 2-4 weeks. Need for long-term oral antibiotic therapy was assessed by weekly culture and sensitivity pattern and status of inflammatory markers (C-reactive protein [CRP], erythrocyte sedimentation rate [ESR]). Patients with femur non-unions were put on derotation bar. And all patients were encouraged to do non weight bearing active and passive physiotherapy of all free joints.

**Table 1**

Age/sex	Site and implant	Type of fracture	Micro-organism	Duration of infection (months)	Procedures
26/M	Femur/ILN	Closed	<i>S. aureus</i>	6	Debridement (2), screw removal
30/M	Femur/ILN	Grade 2	<i>S. aureus</i>	8	Debridement (1)
40/M	Tibia/Fixator	Grade 3B	<i>S. aureus</i>	6	Debridement (2), drilling
25/M	Femur/K-nail	Closed	<i>S. aureus</i>	9	Debridement (1)
30/M	Tibia/ILN	Grade 3A	<i>Proteus</i>	7	Debridement (1), dynamisation
18/M	Femur/ILN	Grade 3A	<i>S. aureus</i>	6	Debridement (1), screw removal
46/F	Femur/ILN	Grade 3A	<i>P. aeruginosa</i>	6	Debridement (2)
22/M	Tibia/ILN	Closed	<i>S. aureus</i>	7	Screw removal
36/M	Femur/K-nail	Grade 2	Poly	7	Debridement (2)
41/M	Tibia/ILN	Closed	<i>S. aureus</i>	8	Debridement (1)
38/M	Femur/K-nail	Closed	<i>S. aureus</i>	7	Debridement (2)
27/M	Femur/ILN	Grade 2	<i>S. aureus</i>	10	Screw removal (2)
45/M	Tibia/Fixator	Grade 3B	Poly	6	Debridement (1), screw removal
39/M	Femur/K-nail	Closed	<i>S. aureus</i>	7	Debridement (1)

*S. aureus*: *Staphylococcus aureus*, ILN: Interlocking nailing, K-nail: Kuntscher-nail, *P. aeruginosa*: *Pseudomonas aeruginosa*, M: Male, F: Female



**Figure 1: Infected non-union exposed, thoroughly debrided, over-reaming of medulla and copious saline lavage done**



**Figure 2: Materials for antibiotic nail preparation, antibiotic nail being prepared and inserted**

### Follow-up

Patients were asked to visit outdoor once in a month for first 3 months followed by once in 2-3 months later on. During each follow-up visit patient underwent clinical and radiological evaluation by standard anterior-posterior, lateral and oblique X-rays to assess the status of non-union. Status of infection was assessed by clinical history and hematological investigations (ESR, CRP, differential count, total count) to check the level of inflammatory markers.

All patients were assessed at 6 weeks to know the status of infection control and bridging callus. Those patients who show signs of infection control and evidence of callus formation at 6 weeks were continued with antibiotic nail till fracture union. And patients with infection control and without any signs of bridging callus underwent antibiotic nail removal followed by exchange intramedullary ILN.

All patients during follow-up were assessed to know the rate of infection control, rate of fracture union, duration for infection control and secondary procedures required to achieve fracture union.

### RESULTS

Outcome of the study analyzed in terms of success and failure. Success cases are those where complete clinical and radiological union occurred. Failure cases are those where non-union failed to achieve union with or without control of infection. Average duration of follow-up was 14 months, ranging from 6 months to 20 months. Most common micro-organism isolated in our study was *S. aureus*.

Out of 14 cases in our study that underwent antibiotic cement nail insertion 13 cases (92%) achieved infection control at an average duration of 6 weeks (Chart 1). Out of these 13 cases 3 patients (23%-success) had radiological signs of callus formation and these patients were continued with antibiotic nail till fracture union. Consequently all the 3 patients achieved bony union by mean duration of 6 months and underwent cement nail removal. One patient with active infection at 6 weeks was continued with antibiotic nail and was put on culture sensitive antibiotics.

Rest 10 cases (77%) with no evidence of callus formation at 6 weeks underwent cement nail removal and definitive fixation by intramedullary nail along with autogenous cancellous bone grafting (Chart 2). Out of ten cases who underwent revision nailing and bone grafting 8 cases (80%-success) achieved bony union at average duration of 5 months post revision nailing. Remaining 2 cases (20%-success) required additional procedures in the form of dynamization to achieve complete union.

Overall (Chart 3), 13 cases achieved infection control and bony union at the last follow-up.

### Failure

One case (7%) of femur non-union where infection was not controlled by 6 weeks failed to achieve infection control at 12 weeks follow-up. Patient underwent cement nail removal and was managed by Papineau method of open dressing and bone grafting. Patient achieved union at 6 months post Papineau procedure.

### Complications

Most common complication in our series was stiffness of the knee joint (5 cases), cement debonding occurred in 3 cases where cement nail retained till fracture union. Cement debonding was managed copious saline irrigation and over reaming the medulla and creation of channel distally for complete removal.<sup>5</sup>

### Case 1

Infected tibia non-union, managed by antibiotic nail insertion. At final follow-up union seen antibiotic nail after removal and healed sinus noted.



### Case 2

Case of infected femur non-union with sinus, managed by antibiotic nail, after 6 months union seen, clinically healed scars noted.



### DISCUSSION

Management of infected non-union is a challenging task for orthopedic surgeon. The increasing trend of high velocity road traffic accidents and consequent open fractures and increased

use of foreign bodies for fracture fixation are some of the causes for incidence of infected non-unions. Pathophysiology of infected non-unions of long bones after intramedullary nailing includes spread of infection along the intramedullary canal.<sup>6</sup> Presence of foreign body and the biofilm makes the eradication of infection impossible by systemic antibiotics. Presence of long term infection along with repeated attempts of debridement creates excessive fibrosis in and around non-union site which hinders antibiotic reach.<sup>7</sup>

Traditionally infected non-unions are treated by repeated debridement's, implant retainment and long-term antibiotic therapy, implant removal and stabilization with external (Ilizarov, LRS) or internal stabilization, Papineau procedure. All these methods are associated with high incidence of joint stiffness, muscle contractures, pin site infection, long term hospital stay.

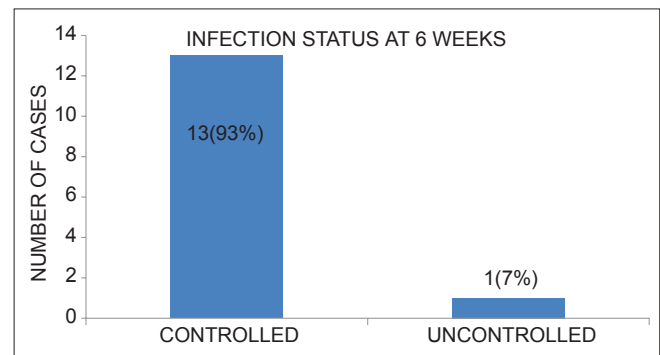


Chart 1

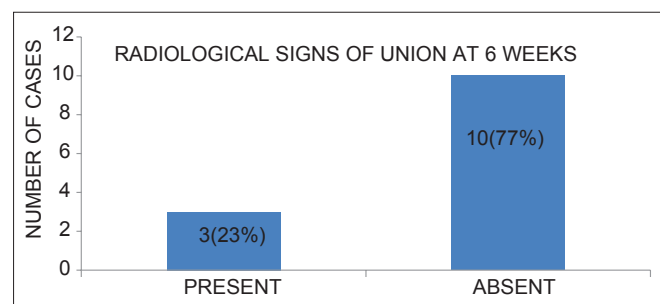


Chart 2

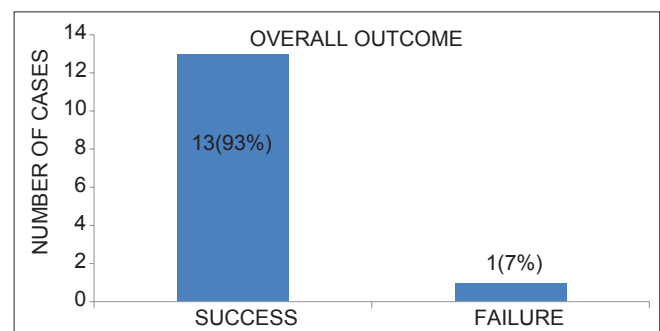


Chart 3



Antibiotic cement nails technique first described by Paley and Herzenberg<sup>8</sup> later by Thonse and Conway. Antibiotic cement nails prepared using polymethylmethacrylate bone cement and heat stable broad spectrum antibiotics. Commonly used antibiotics are vancomycin, tobramycin and gentamycin.<sup>9</sup> Use of ender and K-nail for cement nail preparation has been described in many studies.<sup>10</sup> Cement nails by virtue of their intramedullary position provides high local antibiotics to the concentration of >200 minimal inhibitory levels. Main advantages of antibiotic nails are negligible systemic side effects, easy method of insertion and less time for intraoperative preparation.<sup>5</sup>

Thonse and Conway in their study where infected non-unions were managed by antibiotic nails they achieved infection control in 85% of cases and union was seen in 84% cases. Around 27% patients required additional procedures for infection control and union. Most common complication in their series was cement debonding. Our study differs from their study where in antibiotic cement ILNs were used. Infection control of our study (92%) is comparable to their study (85%).

Sancheti *et al.* in their study where infected non-union with different gap width was managed by antibiotic nail achieved infection control in all cases where bone loss was >6 cm, they also achieved union with antibiotic nail in 3 cases where bone loss was <3.2 cm rest requiring revision nailing and bone grafting. Rate of infection control and union rate of our study are comparable to the results of this study.

In our series, one failed case had pseudomonas infection. And most common complication was joint stiffness thought to be due to unstable fixation provided by K-Nail and V-Nail. Next common complication was cement debonding. Main limitations of our study were small study population due to narrow inclusion criteria and given the small number of failures we were unable to draw conclusion regarding predictors of outcome.

## CONCLUSION

Antibiotic impregnated intramedullary nailing is a simple, very effective method of management of infected non-unions with bone loss <4 cm where it offers best results in terms of infection control (92%). The method by itself achieved bony union in only 23% cases, rest of patients require revision nailing along with bone grafting to achieve union. 20% cases required additional procedures, to achieve union after revision nailing. Hence, we recommend use of antibiotic cement nails for control of the intramedullary infection and this should be, followed by revision nailing, thereby complications (cement debonding, stiffness) reduced and high-success rate achieved with the procedure.

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# Outcome Results of Programmatic Management of Drug Resistant Tuberculosis in 84 Patients From North Coastal Andhra Pradesh

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## Abstract

**Background and Objectives:** In order to achieve “universal access” targets Revised National Tuberculosis Control Programme (RNTCP) control program is deploying rapid diagnostics like line probe assay (LPA), liquid cultures and Gene Xpert for rapid diagnosis of multidrug-resistant tuberculosis (MDRTB). This study is undertaken to highlight the advantages of LPA in early detection of MDRTB and initiation of Category (CAT) IV regimen. It also analyses treatment outcome results of 84 patients of MDRTB under programmatic management of drug-resistant tuberculosis (DR-TB).

**Materials and Methods:** A retrospective analytic study of 84 patients of MDRTB belonging to 3 districts of North coastal Andhra Pradesh, admitted at DR-TB center, Government Chest Hospital, Visakhapatnam between May 2011 and December 2011. The demographic details, meantime delays for diagnosis and treatment, sputum smear and culture conversion results, adverse drug reactions (ADR), treatment outcome results are analyzed.

**Results:** The mean time interval for MDR diagnosis was 6.144 days in 82 patients. There is a mean delay of 13.32 days in 79 patients in initiation of CAT IV regimen. Cure rate was 53.57%, default rate 13%, the death rate 25% and ADR frequencies 33% and none had extensive DR-TB.

**Conclusion:** Rapid diagnostics like LPA will reduce the delay in MDR diagnosis and treatment. This will reduce the death rate in long-term. Default rate can be reduced by intensifying health education, strengthening family support and improving nutritional status.

**Keywords:** Line probe assay, Multidrug-resistant tuberculosis, Programmatic management of drug-resistant tuberculosis, Universal access

## INTRODUCTION

India is home to over 25% of world's tuberculosis (TB) cases and ever since government of India started implementing DOTS Strategy under Revised National TB Control Program (RNTCP) since 1997, the country has come a long way.<sup>1</sup> The entire country is covered with DOTS by 2006 and treatment success rate improved since then. However, the emergence of multidrug-resistant tuberculosis (MDRTB) has become a challenge all over the world, and it is creating an obstacle to the effective management of TB in our country as well.

World Health Organization (WHO) estimates that between 2,20,000 and 4,00,000 MDRTB occurred among TB cases notified in the world in 2011. About 60% of these occurred in Brazil, Russian Federation India, China, and South Africa alone (BRICS Countries). India has the second highest burden of MDRTB cases following China.<sup>2</sup> RNTCP started a WHO recommended DOTS PLUS program in a phased manner for the systematic treatment of MDRTB in 2007. By Feb 2013, programmatic management of drug-resistant tuberculosis (PMDT) services were available in 35 states of the country (including Union Territories), 638 districts covering a population of 1089 million (92%)



and were rapidly scaled up to include remaining districts by 24<sup>th</sup> March 2013.<sup>3</sup>

As per the drug resistance surveillance surveys in Gujarat, Maharashtra and Andhra Pradesh, estimated proportion of MDRTB is 2.1% (1.5-2.7%) in new TB cases and 15% (13-17%) in previously treated cases.<sup>4</sup> Global data show that 32% of relapse cases actually have MDRTB.

Until recently, RNTCP relied on conventional Lowenstein Jensen culture (LJC) and drug susceptibility tests (DST) for the diagnosis of DRTB cases. By December, 2009 there were only 14 such laboratories across the country, validated and certified by RNTCP for conducting LJC and DST, where the mean time to detect DRTB was 3-4 months. Newly developed molecular-based genotypic methods have advantages over conventional phenotypic cultures in terms of both accuracy and turn-around time. A multisite validation study conducted at three-state level reference laboratories in different regions in India by foundation for innovative diagnostics (FIND) showed that in addition to a higher proportion of interpretable results with line probe assay (LPA) compared to LJC and DST (94% vs. 80%) it demonstrated an overall sensitivity and Specificity of LPA for detection of resistance to rifampicin which was high at 96% and 99% respectively.<sup>5</sup> These findings are similar to a large meta-analysis by Ling *et al.* in 2008.<sup>6</sup> Hence it is concluded that routine use of LPA can not only reduce the time to diagnose rifampicin and/or isoniazid resistant TB, it can also enable earlier initiation of the patients on standard drug regimen. Thirdly it reduces the chances of transmission of DR strains since a smear positive patient can infect 10-15 persons in a community in a year and can remain infectious for another 2-3 years if left untreated.

In the dynamic transmission model of TB epidemic in India by Suen *et al.*, important implications of India's transition from a treatment generated MDRTB epidemic toward the transmission generated disease are well discussed.<sup>7</sup> It is observed that improving non-MDRTB cure rates to avoid generating new MDR cases will provide substantial non-MDRTB benefits, but will become less effective in reducing MDRTB prevalence over time because more cases will occur from direct transmissions. It is estimated that by 2015, 42% of new MDR cases are transmission generated. Reducing transmission generated cases requires rapid and accurate MDRTB diagnosis, which is why rapid molecular-based tests are becoming increasingly important. Coinciding with RNTCP Phase III a new strategy of a comprehensive national strategy plan has been developed for 2012-2017 and its new objective is universal access to quality diagnosis and treatment for all TB patients in the community. In order to achieve the

targets under universal access by 2015, the program is deploying rapid diagnostics such as light-emitting diode microscope, LPA, automated liquid cultures, Gene Xpert for rapid diagnosis of MDRTB.

Under Phase III, PMDT services were made available for three districts in North Coastal Andhra Pradesh (NCAP) from May, 2011 and for the first time in Andhra Pradesh, MDRTB is diagnosed using LPA as a diagnostic tool. The present study analyses the treatment outcome results of an MDRTB cohort of 84 patients under PMDT guidelines. The patients belonging to three districts of NCAP were admitted at the drug-resistant tuberculosis (DR-TB) center, Government Chest Hospital for Communicable Diseases (GHCCD) in the first 8 months after its inception. It also focuses on the advantages of genotype MTBDR plus LPA over the conventional solid culture techniques in the detection of resistance to rifampicin and Isoniazid.

## MATERIALS AND METHODS

In the present study, retrospective analysis was done on a cohort of 84 MDRTB patients who were admitted at the DR-TB center, in the GHCCD, Andhra Medical College, Visakhapatnam, during the period from May 2011 to December 2011.

All the 84 patients consecutively enrolled in the study were diagnosed with MDRTB at the IRL, Hyderabad and RNTCP certified C&DST Laboratory, Visakhapatnam, located in the building of GHCCD. Prior to the diagnosis, all the patients were MDRTB suspects as per the RNTCP strategy at the time of the study, i.e., patients who failed category (CAT) I regimen and CAT II patients whose sputum was positive at the end of 4<sup>th</sup> month or later. The patients belonged to three districts in NACP, Visakhapatnam, Vizianagaram and Srikakulam. The two-sputum samples of the MDR suspects who were sputum positive were collected in Falcon tubes and transported in cold chain from the respective designated microscopy Centre (DMCs), some to RIL, Hyderabad and some to the C&DST Laboratory in our hospital. The C&DST Laboratory is attached to AMC and supported by FIND, WHO and Central RB Division (CTD) through state, and its first accreditation was done in 2011. All the sputum positive samples of the MDRTB suspects were subjected to LPA and results were available in 2-3 days. When the results were inconclusive, the culture was repeated on LJ culture medium, and the culture isolate was tested with LPA. All the follow-up cultures were also tested on LJ medium. All the confirmed MDRTB cases were traced, counseled and referred to DR-TB center, GHCCD for pre-treatment assessment and initiation of CAT IV regimen.

As per the program guidelines, all the patients underwent thorough clinical evaluation including height and weight recording, complete blood count, blood sugar, liver function tests, renal function tests, thyroid stimulating hormone, urine examination, pregnancy test in women of childbearing age group and HIV testing after counseling and Chest X-ray examination.

During the stay at the DR-TB center, which is a 24 bedded ward (12 for males and 12 for females) with air-borne infection control measures in place as per the guidelines, the patients were initiated on CAT IV regimen consisting of 6 (9) Km Ofx Eto Cs Z E/18 Ofx Eto Cs E. Patients were discharged 1-2 weeks after initiation of CAT IV. Trained DOTS Providers arranged through concerned DTO administered the drugs under supervision, counseled the patients and family and took care to identify and refer them to the DTO/DR-TB center in the event of adverse drug reactions (ADRs).

Follow-up sputum smear and culture examination was done at the end of the months 3, 4, 5, 6 and 7 and at 3 monthly intervals from 9<sup>th</sup> month onwards till the completion of treatment (9, 12, 15, 18, 21, 24 months). The sputum smear microscopy was done at the concerned DMC and culture was done on LJ medium at C&DST Laboratory, GHCCD. If any of the cultures in the last 3 quarters was positive, it was followed by monthly culture in the following 3 months. Based on the culture reports of 4<sup>th</sup>, 5<sup>th</sup>, 6<sup>th</sup> months, the Intensive Phase (IP) was extended to 1-3 months.

After discharge from DR-TB center, the respective DTOs reviewed the patients at monthly intervals during IP and 3 monthly intervals during CP until the end of the treatment. Patients were evaluated for clinical improvement, weight changes and possible adverse reactions.

Treatment Outcome results are classified as follows: Cure, defaulter, death, treatment failure, treatment completed, and still on treatment.

### Cure

A patient who has completed treatment and has been consistently culture negative (with at least 5 consecutive negative results in the last 12-15 months). If one follow-up positive culture is reported during the last three quarters, patient will still be considered cured provided this positive culture is followed by at least three consecutive negative cultures, taken at least 30 days apart, provided that there is clinical evidence of improvement.

### Defaulter

A patient whose treatment was interrupted for two or more consecutive months for any reasons.

### Death

A patient who dies for any reason during the course of drug-resistant TB (M/XDR-TB) treatment.

### Treatment Failure

Treatment will be considered to have failed if two or more of the five cultures recorded in the final 12-15 months are positive, or if any of the final three cultures are positive.

### Treatment Completed

A patient who has completed treatment according to guidelines but does not meet the definition for cured or treatment failure due to lack of bacteriological results.

### Still on Treatment

An M/XDR-TB patient who, for any reason, is still receiving their treatment at the time of the submission of the treatment outcome report.

## RESULTS

A total of 84 cases of confirmed MDRTB cases were admitted at DR-TB center, GHCCD, Visakhapatnam between May 2011 and December 2011. Of the 84 cases, 65 were Males, and 19 were females. 63 patients belonged to the age group <45 years, the youngest being 14-year-old. 47 patients lived in urban areas, and 37 belonged to rural areas. The number of patients belonging to Visakhapatnam, Vizianagaram and Srikakulam, were 40, 27, 17 respectively (Table 1).

Of the 84 patients, 16 were CAT I Failure and 68 were CAT II failures. The resistance pattern on LPA showed that 58 patients were resistant to R and H, and 26 patients were

**Table 1: Demographic data and resistance patterns**

Characteristics	Data
Age (years)	
<30	32
30-45	31
>45	21
Residence	
Urban	47
Rural	37
Sex	
Males	65
Females	19
Ratio	3:1
Weight bands (kg)	
16-25	2
26-45	37
>45	25
Resistance patterns on LPA	
Rifampicin (H) only	26 (30%)
Rifampicin and isoniazid (R and H)	58 (70%)

LPA: Line probe assay

resistant to R alone. In 2 cases due to inconclusive LPA results, LJ Inoculations and retesting of culture isolates with LPA was done.

Two patients belonged to the weight band of 16-25 kg, 37 patients to 26-45 kg, and 25 patients to >45 kg.

Definition of smear conversion, culture conversion, time to culture conversion.

### Smear Conversion

Patients will be considered smear converted after having two consecutive negative smears taken at least 1 month apart (Table 2).

### Culture Conversion

Patients will be considered culture converted after having two consecutive negative cultures taken at least 1 month apart.

### Time to Culture Conversion

It is calculated as the interval between the date of MDRTB treatment initiation and the date of the first of these two negative consecutive cultures (the date that the sputum specimens are collected for culture should be used).

The mean time taken from sputum sample collection to MDR confirmation at C&DST Laboratory at GHCCD is 6.144 days (range 1-25 days) in a total of 82 cases. In 2 cases due to inconclusive results on LPA and LJ Culture and reanalysis the time taken was 40 days and 37 days.

For 79 cases, after MDRTB confirmation, CAT IV Regimen initiation at DR-TB center was done in the mean time of 13.32 days (range of 7-30 days). 5 cases had a mean delay of 100 days due to patient's unwillingness to be started on the regimen, lack of family support, etc.

At the end of 3<sup>rd</sup> month, sputum smear conversion occurred in 62 patients, and it remained positive in 11 patients. Culture conversion was observed in 65 patients and eight remained cultures positive. By the end of 3<sup>rd</sup> month, Deaths and defaulters were nine and two respectively.

**Table 2: Smear and culture conversion at 3<sup>rd</sup> and 6<sup>th</sup> months**

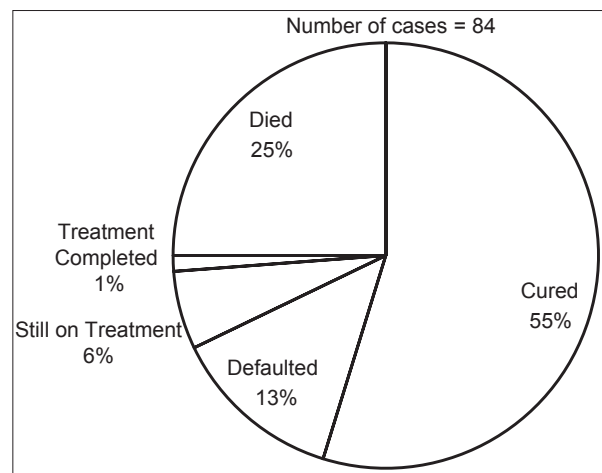
Characteristic	By the end of 3 <sup>rd</sup> month (%)	By the end of 6 <sup>th</sup> month (%)
Smear converted	62 (74)	55 (65)
Smear positive	11 (13)	7 (8)
Culture converted	65 (77)	56 (66.6)
Culture positive	8 (9.5)	6 (7.1)
Defaulters	2 (2)	5 (5.9)
Deaths	9 (10.7)	7 (8.3)

At the end of 6<sup>th</sup> month, smear conversion was observed in 55 patients and smear was still positive in 7 patients. At the same time, culture conversion was seen in 56 patients, and it remained positive in 6 patients. Of these 6 patients, three converted by 7<sup>th</sup> month, one by 9<sup>th</sup> month, one by 12<sup>th</sup> month and the 6<sup>th</sup> patient died. By the end of 6<sup>th</sup> month, deaths and defaulters were seven and five respectively (Figure 1).

Out of the 56 patients who were culture converted by the end of 6<sup>th</sup> month, one patient became culture positive by the 12<sup>th</sup> and 15<sup>th</sup> months. He was declared as "treatment failure" and his sputum sample was sent to national reference laboratories, National Institute for Research in TB Chennai, for second line DST. He was found to be resistant to ofloxacin and sensitive to Kanamycin and hence the DR-TB center Committee replaced ofloxacin with moxifloxacin.

Comorbidities associated in the present cohort were diabetes mellitus in 9 patients and HIV disease in 1 patient. Out of the 9 patients with DM, culture conversion occurred at the end of 3<sup>rd</sup> month in 8 patients and at the end of 4<sup>th</sup> month in 1 patient. During the follow-up months, 1 patient defaulted and one patient died after 9<sup>th</sup> month. The single patient with HIV also got culture converted by 3<sup>rd</sup> month, but the patient died during follow-up after 11 months.

During the course of DOTS PLUS treatment, 28 cases were referred to DR-TB center Committee for management of ADR. Admission was done only in those cases where Observation and/or change of regimen were required. Minor skin reactions like pruritic rash in 2 cases and acne form lesions in one case were observed. Three patients were admitted for breathlessness, and one for hemoptysis, all of them were symptomatically managed. Three patients had joint pains and gastrointestinal symptoms such as nausea, vomiting, diarrhea, dysphagia were observed



**Figure 1: Treatment outcomes of 84 patients enrolled in the study**

in three patients and were managed symptomatically. Peripheral neuropathy was observed in one patient in whom ethionamide was NaPAS. Five patients presented with tinnitus and loss of hearing. They were examined by ENT surgeon and audiometry was done. Kanamycin was replaced by NAPAS in these patients. None of the patients had severe ADR necessitating the total cessation of treatment.

The treatment outcome results were analyzed. 46 out of the 84 cases (53.57%) were cured. Of these cases, one case was a treatment failure but eventually turned "Cured." 21 patients died, and 11 defaulted. All the defaulters were males. Five patients were "Still on Treatment" and one case "Treatment Completed." None was diagnosed with XDRTB.

## DISCUSSION

In the present study of 84 patients, males had a predominance of 77%. 63 out of 84 (75%) belonged to productive age group of <45 years. In our present study, 16 out of 84 (19%) were CAT I Failure and the rest, CAT II Failure. In a similar study by Visakha *et al.* the CAT I/III failures were 12.69%, and the rest were CAT II failures.<sup>8</sup>

Majority (37) of the patients in the present study belonged to weight band of 26-45 kg followed by >45 kg weight band.

In the present study, LPA results showed a mono resistance pattern to rifampicin in 26 out of 84 patients, and the rest were resistant to both H&R. The mean time interval from the specimen collection to obtaining LPA result was 6.144 days (in 82 cases). After confirmation of MDRTB, there was a mean delay of 13.32 days in 79 cases in the initiation of CAT IV regimen at DR-TB center. Five cases had a mean delay of 100 days due to patient's reluctance and other personal reasons.

In a multisite validation study of LPA by Raizada *et al.*, the average delay was 11 days (Range 1-76 days).<sup>5</sup> In another DOTS PILOT study by Singla *et al.*, there was a mean delay of 5 months in establishing a diagnosis of MDRTB when IJC and DST were used.<sup>9</sup> When BACTEC was used, the mean delay was reduced to 2.8 months. In the same study, after diagnosis of MDRTB there was a mean delay of 3.3 months in initiating treatment. Hence the use of LPA can substantially reduce the time to diagnosis of MDRTB, and it enables earlier commencement of standard treatment, thereby preventing transmission of MDRTB strains in the community.

Different studies have shown that sputum culture conversion rate varied from 74% to 92%. In the present study 65 of 84 (77%), were culture converted by the end

of 3<sup>rd</sup> month 56 of 84 (66.6%) by the end of 6<sup>th</sup> month. It shows that the majority become non-infectious by end of 3<sup>rd</sup> month. The 5 patients who remained culture positive by the end of 6<sup>th</sup> month converted in the later months (7-12<sup>th</sup> months).

By the end of 3<sup>rd</sup> month, the deaths and defaults were 9 and 2 cases respectively and by the end of 6<sup>th</sup> month they were 7 and 5 cases. It shows that most deaths (16 of 21) occurred before 6 months. Since this study had the first batch of pooled up patients in the North coastal districts who were waiting to be diagnosed and treated for MDRTB, the early deaths indicate extensive damage to lungs of the patients. Defaulter rate (7 of 11) too was more in the first 6 months.

ADR were reported in various studies with a frequency of 19-72%. The present study had 28 cases referred to DR-TB center for the management of ADR (33%). Only 6 patients (7%) had major ADR. In one patient with ethionamide induced peripheral neuropathy, the drug was replaced by NAPAS and in 5 patients with kanamycin induced 8<sup>th</sup> nerve toxicity, the drug was replaced by NAPAS.

Although psychotic reaction due to cycloserine was observed in a significant number of cases in the Singla *et al.* and Visakha *et al.* studies, where the drug had to be terminated, the present study did not have any patient with such psychotic or depressive reactions.

Analysis of treatment outcome results showed that cure rate was 53.57%. Various studies worldwide demonstrated a cure rate varying from 38-100%. Our cure rates are lower when compared to the 66% and 61% of Joseph *et al.* and Singla *et al.* studies respectively.<sup>9,10</sup> Yet our Cure Rates are higher than the 39% of Visakha *et al.* and 37% of Thomas *et al.* and 39% of Jain *et al.*<sup>8,11,12</sup> The defaulter rate of 11 of 84 (13%) and the death rate of 21 of 84 (25%) in the present study explains the lower cure rates (53%) (Table 3). The defaulter rate and death rates in our present study are similar to many other studies across India. When enquired into the reasons for defaulting, it is observed that the defaulted patients lacked family support, were

**Table 3: Outcome of MDRTB in different studies a comparison**

	Cure rate (%)	Default rate (%)	Death rate (%)
Present study	54	13	25
Thomas <i>et al.</i>	37	24	13
Singla <i>et al.</i>	61	18	19
Visakha <i>et al.</i>	39	26	21
Joseph <i>et al.</i>	66	13	8
Jain <i>et al.</i>	39	23	19

MDRTB: Multidrug-resistant tuberculosis



reluctant to consume a large number of pills for a period of 24 months and sometimes migration was the cause. Some had very low nutritional status and did not want to go on with the treatment and attributed minor adverse effects to the drugs.

The diabetics and HIV patients in the present study had culture conversion by 3<sup>rd</sup> month except in one patient. It indicates that the CAT IV regimen is equally efficient in MDRTB patients with comorbidities. It is also observed that none of the females defaulted although the death rates are almost equal in both sexes. The zero-default rate in female patients is probably because of absence of risk factors like smoking and alcoholism and also women in general are believed to be more vigilant and compliant with drugs.

The overall treatment success rate is 48% according to the data available from 60 countries across the world.<sup>2</sup> The global target of treatment success rate is 75% which can be achieved with rapid scale-up of RNTCP services and more number of certified laboratories adopting rapid diagnostic methods. RNTCP strategy of case detection also has changed with the new A, B, C criteria for an MDR suspect.<sup>13</sup> This will also help in the detection of disease in early stage before permanent lung damage occurs.

To make the patients more knowledgeable about their condition and for better adherence, strong health education to the patient as well as the family members is highly important. More intense monitoring and early identification and management of ADR also help to reduce default rates which will have an impact on the success rate.

This study had few limitations that it is a small cohort, and it was in the early months of PMDT services at our hospital. Therefore, the study group was largely made up of pooled up patients with MDRTB, which may have had an impact on the treatment outcome. There were also some initial operational difficulties because of which this study lacks data of BMI, radiological features and history of contact details.

## CONCLUSION

The cure rate with PMDT in the present study is 53.57% which is above overall treatment success rate (48%). The global target of 75% can be achieved with widespread use of rapid diagnostics like LPA, which will reduce the time for diagnosis and treatment of MDRTB. This will help in reducing death rate in the long term which will have an

impact on success rate. The default rate can be further reduced by intensifying health education, improving family support and nutritional status.

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# Hematological Survey in Pre-school Children with Special Reference to Iron Deficiency Anemia

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## Abstract

**Introduction:** Anemia in children is a common health problem in developing countries. The most vulnerable group is the pre-school children living in rural as well as slum areas. The current study gives emphasis on utility of complete blood count for screening, and its correlation with Iron profile studies for detection of iron deficiency anemia in pre-school children.

**Aims and Objectives:** To study the hematological profile and prevalence of iron deficiency anemia in children aged between 1-5 years.

**Materials and Methods:** A total number of 112 cases attending Rajah Muthiah Medical College Hospital Pediatrics Outpatient Department during the period of July 2007-July, 2009 were included in the present study. Venous blood samples were collected by venepuncture into containers with di-potassium ethylenediaminetetraacetic acid. All samples were analyzed for hematological parameters (erythrocyte count, hemoglobin, hematocrit, mean corpuscular volume [MCV], mean corpuscular hemoglobin [MCH] concentration [MCHC] and red cell distribution width [RDW]). Serum sample of randomly selected 12 children were analyzed for iron profile studies (serum ferritin [S. ferritin], serum iron [S. iron], total iron binding capacity [TIBC] and percentage saturation).

**Results:** A total of 112 cases were included in the study. The prevalence of anemia was found to be 73.2%. Out of 82 anemic pre-school children, 47 (57.31%) were found to be males and 35 (42.68%) were found to be females. Thus, male to female ratio in the present study was found to be 1.3:1. Hemoglobin value of pre-school children was <11 g/dl in 82/112 cases (73.2%). Mild degree of anemia was most common (40.2%), followed by moderate degree (22.3%). Majority of the cases (54%) showed reduced hematocrit reduced MCV, MCH and MCHC were noticed in 73.2%, 61.6% and 54.5% respectively. Increased RDW was noticed in 58.9 % of the cases. Classification of anemia was done using MCV and RDW and found that 58.9% came under microcytic heterogeneous type due to iron deficiency. Iron profile studies in 12 cases showed reduced S. ferritin (91.7%), S. iron (75%) and percent saturation (75%). TIBC was increased in 66.7% of the cases.

**Conclusion:** A significant correlation exists between hemoglobin, hematocrit, MCV, MCH, MCHC and RDW. Hemoglobin concentration below 11 g/dl in pre-school age group was found to be an effective screening test for selecting patients for further evaluation. Among the iron profile studies, S. ferritin measurement is the most sensitive indicator of iron deficiency.

**Keywords:** Anemia, Hemoglobin, Mean corpuscular volume, Red cell distribution width, Serum ferritin

## INTRODUCTION

Anemia is one of the common problems encountered in clinical medicine. However, anemia is not a disease but rather the expression of an underlying disorder or disease.<sup>1</sup> Anemia is defined as a low-hemoglobin concentration or red blood cell mass compared to the age-specific norms.<sup>2</sup> Anemia is functionally defined as a decrease in the

competence of blood to carry oxygen to tissues, thereby causing tissue hypoxia.<sup>1</sup>

Anemia in children is a commonest health problem in developing countries and frequent laboratory abnormality encountered in children.<sup>3,4</sup> The most vulnerable group regarding health and nutritional status are the pre-school children living in rural as well as slum areas, who are victims

of undernourishment.<sup>4</sup> Preschool denotes children aged 1-5 years.<sup>5</sup> Pre-school age is when brain development and physical growth is at its maximum acceleration, hence its importance.<sup>4</sup>

Iron deficiency is currently the most widespread micronutrient deficiency with an estimated prevalence of 43%.<sup>6</sup> Most children with anemia are asymptomatic and have abnormal hemoglobin or hematocrit level on routine screening. Anemia in infancy and early childhood is associated with behavioral and cognitive delays, including impaired learning, decreased social achievement, and low scores on tests of mental and motor development.<sup>5</sup> Given the detrimental long term effects, and high prevalence of nutritional deficiency, its prevention in early childhood is an important public health issue.<sup>2</sup>

The complete blood count is a test frequently done on children presenting to pediatric outpatient department, usually for consultation and the same can be utilized to screen for iron deficiency anemia at no additional cost. Additional biochemical tests may be done for confirmation after screening tests in these cases. The present study is on hematological parameters with special reference to iron deficiency anemia among pre-school children attending Rajah Muthiah Medical College and Hospital hailing from the rural community in and around Chidambaram, Tamil Nadu.

## MATERIALS AND METHODS

A total number of 112 cases attending Rajah Muthiah Medical College and Hospital Pediatrics Outpatient Department during the period of July 2007-July, 2009 (2 years) were included in the present study and was cleared by Institutional Ethics Committee.

### Sample Collection for Hematological Parameters

Blood was withdrawn from an ante cubital vein by means of dry sterile 5 ml, disposable plastic syringe with a needle of 20-gauge after preparing the cubital fossa with a sterile swab. 2 ml of blood was withdrawn, slowly. Immediately blood is transferred to sterile glass bottle with di-potassium EDTA as anticoagulant.

Sample was analyzed in an automated cell counter (MODEL and COMPANY: MYTHIC 18, ORPHEE SA, C2 DIAGNOSTICS, FRANCE) for complete blood counts (erythrocyte count, hemoglobin, hematocrit, mean corpuscular volume (MCV), mean corpuscular hemoglobin concentration (MCHC), red cell distribution width (RDW), Reticulocyte count and platelet count).

### Sample Collection for Iron Profile Studies

The blood in the bottle without anticoagulant was allowed to clot without disturbances for 30-60 min at room temperature. Once the stable clot was formed, the serum separates out. The serum was taken through long pasteur pipette and centrifuged at 3000 RPM for 10 min, and the supernatant was taken into a sterile plastic radioimmunoassay tube and stored at  $-20^{\circ}\text{C}$ . Sample was analyzed in an automated biochemical analyzer (equipment: Immulite 1006 systems, Diagnostic Product Corporation, USA and IMOLA-RANDOX) for iron profile studies (serum ferritin [S. ferritin], serum iron [S. iron], total iron binding capacity [TIBC] and percent saturation).

### Inclusion Criteria

- Randomly selected children attending pediatric outpatient department aged 1-5 years during study period.

### Exclusion Criteria

Children with:

- Acute infections
- Communicable diseases like HIV, tuberculosis hepatitis
- Other major and chronic illness. Hematinics support
- History of recent blood transfusion
- Known cases of hemoglobinopathies.

## RESULTS

112 pre-school children were included in the study. 82 out of 112 cases (73.2%) were found to be anemic as per WHO definition. Out of 82 anemic pre-school children, 47 (57.31%) were found to be males and 35 (42.68%) were found to be females. Thus, male to female ratio in the present study was found to be 1.3:1. 60 cases (53.6%) had hematocrit  $<33\%$ . Hemoglobin value of pre-school children was  $<11$  g/dl in 82/112 cases (73.2%), and it was  $\geq 11$  g/dl in 30/112 cases (26.8%). Among pre-school children, a mild degree of anemia (9-11 g/dl) seen in 37.5% of cases, moderate degree of anemia (7.0-9.0 g/dl) seen in 22.3% of cases and 10.7% of cases were severely anemic ( $\leq 7.0$ ). 82/112 (13.2%) had MCV below 80 fl, 15/112 (13.4%) had MCV within the normal range and 15/112 (13.4%) had MCV more than 100 fl. 69/112 (61.6%) pre-school children had mean corpuscular hemoglobin (MCH) below 25.9 pg, 37/112 (33.03%) had MCH within normal range (26.0-34.9 pg) and 6/112 (5.4%) had MCH more than 35.0 pg. 61/112 (54.5%) pre-school children had MCHC below 30.9 g/dl, 49/112 (43.8%) had MCHC within normal range (31.0-36.0 g/dl) and 2/112 (1.8%) had MCH more than 36.1 g/dl. 73.2 % of preschool children had decreased MCV ( $<80$  fl). Classification of anemia was made on the basis of comparison of MCV and RDW with number of cases in each group (Figure 1).

Comparison between parameters of iron profile studies and between MCV, RDW and S. ferritin, were done in 12 randomly selected cases and illustrated in Figures 2 and 3 respectively.

## DISCUSSION

Anemia in pre-school age group was defined and classified using WHO criteria (Hgb <11 g/dl). Degree of anemia was

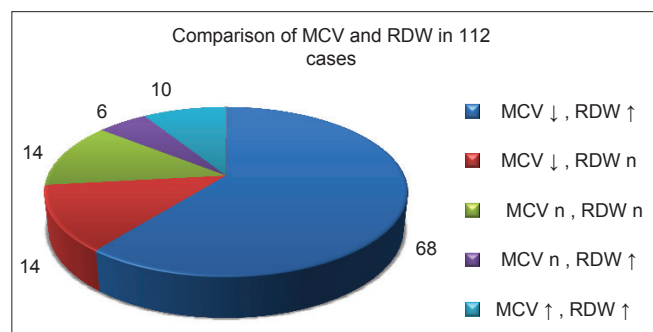
classified as mild ( $9.0 \leq 11.0$  g/dl), moderate ( $7.0 \leq 9.0$  g/dl) and severe ( $<7$  g/dl).<sup>6</sup> In the present study, prevalence of anemia was found to be 73.2% which was in concordance with other similar studies as shown in Table 1.

Sex distribution of anemia was compared with studies conducted by Gomber *et al.*,<sup>8</sup> Kapur *et al.*<sup>18</sup> and Halileh *et al.*<sup>19</sup> as shown in Figure 4.

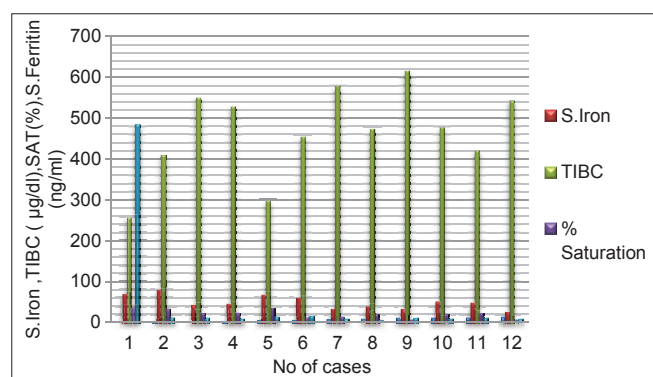
Degree of anemia was classified as mild ( $9 \leq 11.0$  g/dl), moderate ( $7 \leq 9.0$  g/dl) and severe ( $<7$  g/dl). Mild degree of anemia was most prevalent (40.2%) in the present study followed by moderate (22.3%) and severe anemia (10.7%). The findings were in accordance with studies conducted by Gomber *et al.*<sup>8</sup> and Chakravarty and Ghosh.<sup>13</sup> Comparison of MCV and RDW were done and found out that 73.2% of children had decreased MCV ( $<80$  fl) and 58.9% had increased RDW, which correlated with studies conducted by Patton *et al.*,<sup>14</sup> Oski *et al.*<sup>11</sup> and Pusic *et al.*<sup>15</sup>

Classification of anemia was made on the basis of MCV and RDW which was proposed by Bessman *et al.*<sup>12</sup> Anemia's are classified into six types - microcytic heterogeneous, microcytic homogeneous, normocytic homogeneous, normocytic heterogeneous, macrocytic homogeneous and macrocytic heterogeneous. In the present study, 68 pre-school children had microcytic heterogeneous type of anemia (MCV ↓, RDW ↑) due to iron deficiency.

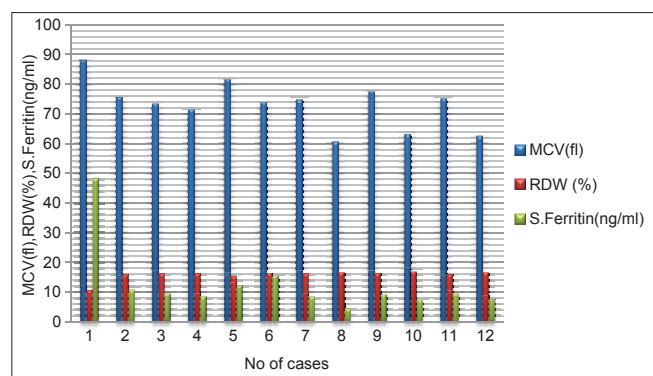
Comparison of Hgb and S. ferritin showed decreased S. ferritin in all stages of iron deficiency anemia and may be the first indication of developing iron deficiency anemia.<sup>6</sup> In the present study, all pre-school children with decreased Hgb had decreased S. ferritin (100%). This is in



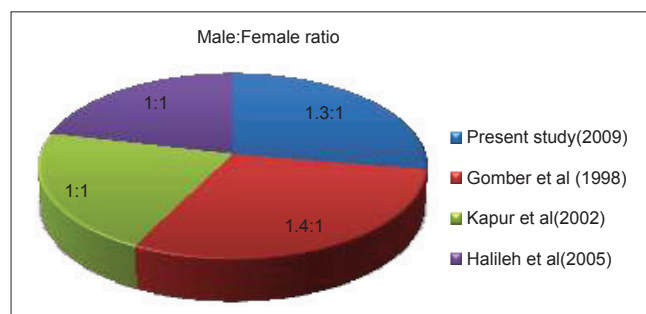
**Figure 1: Comparison of mean corpuscular volume and RDW in 112 cases. (↑ - increased, ↓ - decreased, n - normal)**



**Figure 2: Comparison of Iron profile study in 12 cases**



**Figure 3: Comparison between mean corpuscular volume (MCV), red cell distribution width (RDW) and serum ferritin (S. ferritin). Comparison of MCV, RDW and S. ferritin values in each case showed two patterns. They were: (1) MCV ↓, RDW ↑, S. ferritin ↓. (2) MCV n, RDW n, S. ferritin n (↑ - increased, ↓ - decreased, n - normal)**



**Figure 4: Sex distribution of anemia**

**Table 1: Comparison of prevalence of anemia**

Authors (year)	Prevalence (%)
Herbert <i>et al.</i> <sup>7</sup> (1998)	72.5
Gomber <i>et al.</i> <sup>8</sup> (1998)	76
National Family Health Survey <sup>9</sup> (1998-1999)	74
Villalpando <i>et al.</i> <sup>10</sup> (2003)	72
Present study (2009)	73.2



concordance with Palafox *et al.* (2003), who concluded that comparison of S. ferritin and HgB can be used for detecting iron deficiency anemia.<sup>16</sup> Comparison of MCV, RDW and S. ferritin showed results similar to studies conducted by Hutcheson (1970) and Carlos *et al.* (2001), reported that decreased MCV and increased RDW along with decreased S. ferritin, increased TIBC, decreased S. iron and percent Saturation are confirmatory of iron deficiency anaemia.<sup>17,18</sup>

## CONCLUSION

One of the major areas for improvement in primary health care is prevention of nutritional deficiency because it has been associated with delay in psychomotor development especially in pre-school age. Appropriate screening and subsequent diagnostic testing will allow most cases of anemia to be diagnosed at the earliest. Basal blood parameters are mandatory before treating children with anemia to avoid unwanted side effects. In the present study, a significant correlation was observed between hemoglobin, hematocrit, MCV, MCH, MCHC, RDW and biochemical parameters such as S. iron, TIBC, percent saturation and S. ferritin. HgB, MCV and RDW alone can be utilized for screening and classifying anemias even before doing peripheral smear or biochemical investigations. S. ferritin measurement is the most sensitive indicator of iron deficiency, which is decreased in all stages of iron deficiency anemia and, it is the first indicator of developing iron deficiency anemia even before the drop in hemoglobin. S. iron, TIBC and percent saturation determinants are also of help in the diagnosis of iron deficiency anemia along with S. ferritin.

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# Changing Pattern of Acute Intestinal Obstruction in Western UP Region: An Observational Study

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## Abstract

**Background:** The aim was to study the changing pattern of acute intestinal obstruction in western UP region, India.

**Materials and Methods:** An observational study conducted at Teerthanker Mahaveer Medical College and Research Center, Moradabad, which is a tertiary care level teaching hospital. Patients with clinical, pathological and radiological evidence of acute intestinal obstruction were included in this study. No discrimination of patients was made based on age and sex. Patients were treated accordingly based on the severity, ranging from conservative to surgical laparotomy.

**Results:** A total of 58 patients with intestinal obstruction were admitted and treated. The mean age of the study population was  $40.07 \pm 8.04$  years. Post-operative adhesions were found in 29 patients, abdominal tuberculosis in 19, and hernia in 10 patients. We could notice clear cut demarcation in the type of intestinal obstructions and socio-economic status of the patients.

**Conclusion:** We concluded the study by analyzing the fact that adhesive obstruction are the commonest cause of acute intestinal obstruction and hernias were the least common, which reflects the changing habits of patients to take medical advice before the case becomes complicated.

**Keywords:** Adhesions, Etiology, Hernias, Intestinal obstruction, Tuberculosis

## INTRODUCTION

Acute intestinal obstruction is considered to be most common surgical emergency across the globe with very high morbidity and mortality.<sup>1-3</sup> Among the most common causes post-operative adhesions ranks the list, as noticed by eminent surgeons.<sup>4-6</sup> Although in other part of the world strangulated hernias to be the most common underlying cause of acute intestinal obstruction.<sup>7,8</sup> This dogma is attributed to unawareness, low socio-economic status and operation fear. During the last 5 years, a change in the etiology has been noted in the developing countries.<sup>9,10</sup>

## MATERIALS AND METHODS

A prospective study of 58 patients, presented with acute intestinal obstruction, admitted and evaluated with pathological, radiological and clinical evidence of acute

intestinal obstruction surgery department, not taking in consideration of age, sex and socioeconomic status of the patient. However we separated patients of western UP region for study point of view in which their permanent address was noted to locate their ancestry. Surgical emergency department informed beforehand to send such patients to the authors concerned for their studies point of view. Nursing staff was instructed for immediate fluid and electrolyte resuscitation, and each and every necessary investigation were done before surgery. Patients who underwent laparotomy earlier were put on conservative management. Failure of relief of by conservative treatment for more than 3 days was followed by laparotomy. Patients with clinical history of tuberculosis were also kept on conservative treatment. The data collected and submitted to statistical evaluation. The submitted data were also presented in college Research Committee Meeting, and Ethical Committee approval was also taken.

## RESULTS

Patients of 14-72 years of age with acute bowel obstruction presentation were included in this study. Among 58 patients 43 were males, and 15 were females. In 49 patients the site of obstruction was in the small intestine; while in 9 patients the site of obstruction was the large intestine. In descending order the symptoms that were noted, distension of the abdomen in 51 patients, constipation 52 patients, pain in the abdomen 43 patients, vomiting 42 patients, and dehydration 39 patients. Preliminary investigations like pathological, biochemical, radiological and clinical evaluation were noted. On radiological examination, multiple air-fluid levels were noted in 51 patients. 2 out of 58 patients showed some features of tuberculosis in chest X-ray. Remaining patients who were not amenable to conservative treatment were performed an exploratory laparotomy. Overall 47 patients were operated. In this study, we found diverging trends, if compared with causes of acute intestinal obstruction about 8-10 years back. Today there are most patients with adhesive obstructions, while in previous times it was mainly due to strangulated hernias. Based on the underlying cause of intestinal obstruction treatment modality ranged from simple conservative treatment to resection of bowel loop, followed by end to end anastomoses.

## DISCUSSION

Acute abdomen is the commonest life-threatening emergencies across the globe.<sup>1,11</sup> In the last decade there is felt an obvious change in the etiopathogenesis of intestinal obstruction. Studies conducted in a recent past showed strangulated hernias as the most common cause of intestinal obstruction. Recent studies<sup>12,13</sup> have found definitive change from strangulated hernia to adhesive obstruction as the most common cause of intestinal obstruction. This study is also done to explore the common causes of acute intestinal obstruction in western UP region. Patient's complaints and presentation in our study are almost similar to the studies of.<sup>14-17</sup> The mean age in our study ( $40.07 \pm 8.04$  years) is a little bit different when compared to the studies conducted by.<sup>17,18</sup>

As can be depicted from our study the most common cause of acute intestinal obstruction is adhesive obstruction, it is contrary to earlier studies when strangulated hernia used to be the most common cause.<sup>17</sup> This change in the etiology of acute intestinal obstruction can be attributed to better paying capacity of patients, better education and better medical facilities available in that region. Awareness of complications caused by

strangulated hernias may be the possible region of elective surgery, as we found in our hospital, where about 62% cases were operated electively.

If we go on exploring the cause why adhesive obstruction was the most common cause of acute intestinal obstruction, it led to the simultaneous increase in exploratory laparotomies. 32 patients in our study already had a history of laparotomies for different causes.

The second most common cause of bowel obstruction reported in our study was tuberculosis, which is in accordance with other studies of same socio-economic status and geographical strata.

## CONCLUSION

From the study conducted in our hospital, we concluded that in Western UP region adhesions are the most common cause of bowel obstruction. Patients are visiting the hospital should be encouraged to get radiological investigations done if they feel common symptoms of acute bowel obstruction, so that elective surgery can be performed.

Secondly the patients should be advised to get pathological and microbiological investigations for tuberculosis done because tuberculosis is emerging as second most common cause of bowel obstruction.

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# A Comparative Study to Evaluate the Efficacy of Oral Dexmedetomidine Versus Oral Midazolam as premedicants In Children: A Prospective, Randomized, Controlled and Double Blind Study

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## Abstract

**Background:** The primary goal of premedication in children is to ease the induction of anesthesia by facilitating a smooth separation from the parents. Oral premedication is widely used in pediatric anesthesia to reduce pre-operative anxiety and ensure a smooth induction. Midazolam is currently the most commonly used premedicant, but alpha-2 agonists – clonidine and dexmedetomidine are now considered as good alternatives to midazolam.

**Materials and Methods:** This study was conducted over a period of 8 months. The aim of this study is to evaluate the efficacy of oral dexmedetomidine (3 mcg/kg) versus oral midazolam (0.5 mg/kg) as premedicants in children undergoing different elective surgeries under general anesthesia. Fifty children, aged between 3 and 10 years were considered for the study, and they were randomly allocated into two groups: Group D (dexmedetomidine group;  $n = 25$ ) or Group M (midazolam group;  $n = 25$ ). Demographic data were comparable in both groups.

**Results:** There was no significant difference in anxiety levels among the 2 groups. But post-operative requirement of rescue analgesic dose, post-operative agitation and shivering were less in the dexmedetomidine group, compared to the midazolam group.

**Conclusion:** We conclude that dexmedetomidine may be an effective oral premedicant prior to anesthesia induction in children compared to oral midazolam, as it resulted in significantly lower post-operative pain, decreased post-operative agitation, less incidence of post-operative shivering, as well as more hemodynamic stability.

**Keywords:** Dexmedetomidine, Midazolam, Premedicants

## INTRODUCTION

Pre-operative anxiety is known to prolong the induction of anesthesia and lead to new-onset of maladaptive behavior in the post-operative period.<sup>1</sup> Premedication in children prior to anesthesia induction provides anxiolysis, facilitate the separation from parents, and lessens the adverse psychological effects of hospital stays. Non-parenteral routes of administration for premedication is preferred in children because they perceive intravenous (IV) or intramuscular (IM) medication as more invasive than the procedure itself. Benzodiazepines like midazolam, lorazepam and diazepam are commonly used agents for

premedication in children to produce anxiolysis, easy separation from the patients and allow IV cannulation and face mask application. According to Kain *et al.*<sup>2</sup> midazolam is currently the most commonly used sedative drug for premedication in children. It has been attributed several beneficial effects such as anxiolysis, amnesia and rapid onset of sedation.<sup>3</sup> Alderson and Lerman<sup>4</sup> compared oral midazolam and oral ketamine as premedication agents in children. In recent times, alpha-2 agonists—clonidine and dexmedetomidine gained much popularity as good pre-medication agents. Bergendahl *et al.*<sup>5</sup> showed that these agents produce good pre-operative sedation, anxiolysis, analgesia and peri-operative hemodynamic stability.

Our study compares the efficacy of oral dexmedetomidine and oral midazolam as premedication agents and their effect on the pre-operative sedation, the ease of separation from their parents, the acceptance for IV cannulation, face mask application, effect on post-operative agitation, post-operative analgesia and post-operative shivering.

## MATERIALS AND METHODS

The study was conducted in the Pediatric Surgery Operation Theatre, Government General Hospital attached to Rangaraya Medical College, Kakinada between April 2013 and November 2013. After obtaining institutional Ethical Committee's approval and informed consent from the patients' parents, 50 children belonging to American Society of Anesthesiologists (ASA) Grades I and II, of both sexes, aged between 3 and 10 years, were taken up for study. They were randomly allocated to 2 groups Group D and Group M, each comprising of 25 children.

### Inclusion Criteria

1. Children aged between 3 and 10 years
2. ASA Grade 1-2
3. Children without other co-morbidities
4. Children undergoing elective surgeries only.

### Exclusion Criteria

1. Children with chronic pain and central nervous system disorders
2. Gastrointestinal disorders that affect drug absorption
3. Previous reactions to dexmedetomidine or benzodiazepines
4. Patients with ASA grade >2
5. Patients with other co-morbidities.

Group D children received dexmedetomidine 3 µg/kg orally 45-60 min prior to anesthesia induction.

Group M children received midazolam 0.5 mg/kg orally 45-60 min prior to anesthesia-induction, maximum dose being 15 mg.

In both groups, the required dosage of the injectable form of both the drugs was mixed with 3 ml of honey to make them palatable.

Baseline parameters like heart rate (HR), noninvasive blood pressure (NIBP), respiratory rate and SPO<sub>2</sub> were recorded in both the groups.

Both groups were given standard general anesthesia with injection glycopyrrolate 10 µg/kg IV, injection ondansetron 0.1 mg/kg IV injection fentanyl 1 µg/kg IV and were

induced with injection thiopentone sodium 5 mg/kg IV, Intubated after giving atracurium 0.5 mg/kg IV with appropriate sized ET-TUBE. Maintained with increments of atracurium, oxygen and nitrous oxide mixture 40:60% and sevoflurane 1-1.5%.

In both groups, we have observed and compared pre-operative sedation, post-operative emergence agitation, post-operative analgesia, intra-operative, post-operative hemodynamics and post-operative shivering.

### Monitoring

In all children HR, SPO<sub>2</sub> monitoring were done continuously, systolic blood pressure, diastolic blood pressure and mean arterial pressure (MAP) were monitored every 5 min, starting from the administration of the drug to initiation of general anesthesia, during intra-operative and up to 2 h in the post-operative period.

### Intra-operatively

Injection fentanyl 1 µg/kg increments were given when there was a considerable rise in HR and NIBP. After surgery, patients were reversed with injection glycopyrrolate 10 µg/kg IV and neostigmine 50-70 µg/kg IV and shifted to the recovery room after complete recovery from neuro-muscular blockade, monitored for 2 h and shifted to the ward.

### Parameters Observed

Parameters observed are pre-operative sedation, Ease of separation from the parents, ease of IV cannulation, the face mask acceptance, postoperative agitation, post-operative pain and post-operative shivering.

### Statistical Analysis

Data analysis for was performed by unpaired Student's *t*-test and Chi-square test. *P* < 0.05 was considered as statistically significant and *P* < 0.0001 was considered statistically very significant.

## RESULTS

### Demographic Data

The demographic profiles of the patients in both groups were comparable with regards to age, sex, ASA class, duration of surgeries (Table 1).

There was no significant difference in anxiety levels among the 2 groups.

Patient's mask acceptance was good for more than 75% of the children in both groups. Parental separation was easy in both groups. About 75% of the children in both the groups were cooperative during IV cannulation.

### Pre-operative Sedation

The sedation was assessed using a 5-point score system (Wilson's score):

1. Completely awake and oriented.
2. Sleepy and drowsy, eyes open.
3. Eyes closed but verbally arousable.
4. Eyes closed but arousable with light physical stimulation.
5. Eyes closed but not arousable with physical stimulation.

The onset of sedation was  $28.4 \pm 13.7$  min in Group M and  $39.5 \pm 14.3$  in Group D. This difference was statistically significant ( $P = 0.0073$ ) (Table 2).

### Post-operative Analgesia

It is measured using Wong-Baker pain scale.

Patients with a score of  $\geq 4$  were administered a rescue analgesic (injection fentanyl  $0.5 \mu\text{g/kg IV}$ ). The number of children requiring postoperative rescue analgesic was significantly higher in Group M than in Group D (14 vs. 8,  $P = 0.0015$ ), which is statistically significant.

### Hemodynamic Parameters

After oral dexmedetomidine there were lower levels of MAP and HR than after midazolam. The difference between the two groups was statistically significant during the intra-operative ( $P = 0.0044$  and  $0.0155$  for MAP and HR respectively) and post-operative periods ( $P = 0.0001$  and  $0.0090$  for MAP and HR, respectively) (0-2 hrs) post operative periods which are statistically significant (Table 3).

### Post-operative Shivering

Shivering did not occur in Group D, but was observed in five patients in Group M. This is statistically significant ( $P = 0.018$ ).

### Post-operative Agitation

Agitation was defined by a total modified objective pain scale score of  $\geq 3$  for these three criteria. The proportion of children with agitation in the first 2 h after surgery was significantly lower in the dexmedetomidine group compared with the midazolam group (4 vs. 8,  $P = 0.0001$ ), which is statically very significant (Table 4).

## DISCUSSION

This study demonstrates clinical advantages of oral dexmedetomidine in both the pre-operative period and during recovery, compared with oral midazolam as a preanesthetic medication in children. Oral premedication does not increase the risk of aspiration pneumonia.<sup>6</sup>

**Table 1: Demographic data**

	Group M (n=25)	Group D (n=25)
Age (years)	$6.9 \pm 1.6$	$6.3 \pm 1.5$
Sex (male:female)	15:10	13:12
Duration of surgery	$33.8 \pm 4.98$	$34.1 \pm 5.56$
ASA I/II	22/3	21/4

ASA: American Society of Anesthesiologists

**Table 2: Pre-operative sedation**

	Group M (n=25) (%)	Group D (n=25) (%)
Sedation score $\geq 3$	7 (27)	4 (17)
at 15 min	13 (53)	11 (43)
at 30 min	5 (20)	7 (30)
at 45 min	0	3 (10)
at 60 min	$28.4 \pm 13.7$	$39.5 \pm 14.3$

**Table 3: Hemodynamic parameters**

	Group M (n=25)	Group D (n=25)
Baseline		
MAP (mmHg)	$87.7 \pm 11.2$	$85.1 \pm 9.8$
HR (bpm)	$107.3 \pm 18.6$	$109.9 \pm 16.2$
Preoperative (after sedation)		
MAP (mmHg)	$76.9 \pm 9.1$	$73.8 \pm 10.9$
HR (bpm)	$102.4 \pm 16.3$	$98.9 \pm 13.4$
Intraoperative		
MAP (mmHg)	$71.3 \pm 9.9$	$62.8 \pm 10.2$
HR (bpm)	$96.1 \pm 19.7$	$83.7 \pm 14.9$
Postoperative (0-2 h)		
MAP (mmHg)	$81.6 \pm 10.7$	$69.2 \pm 8.5$
HR (bpm)	$100.9 \pm 18.3$	$87.4 \pm 16.7$

MAP: Mean arterial pressure, HR: Heart rate

**Table 4: Modified objective pain scale**

Criteria	Character	Score
Tears	Absent	0
	Present, but child can be consoled	1
	Present and child cannot be consoled	2
Movement	Absent	0
	Moderate agitation (does not sit still)	1
	Intense agitation (risk of trauma)	2
Behavior	Sleeping or calm	0
	Grimacing, trembling voice, can be calmed down	1
	Frightened, sticks to parents, cannot be calmed down	2

Premedication with oral dexmedetomidine resulted in significantly better post-operative analgesia compared with oral midazolam. Dexmedetomidine administration was also associated with decreased postoperative agitation. The incidence of post-operative shivering was significantly less after dexmedetomidine. Patients in the dexmedetomidine group had comparatively lower levels of MAP and HR, at desirable levels, during both the intra- and immediate post-operative periods. Onset of sedation was significantly slower

after oral dexmedetomidine compared with oral midazolam. However, the delay in onset of sedation of dexmedetomidine is acceptable if clinical advantages are provided during the peri-operative period.

Schmidt *et al.*<sup>7</sup> concluded that post-operative analgesia was more in children premedicated with Clonidine and dexmedetomidine, compared with the children who were pre medicated with midazolam and the required dose of rescue analgesic was less. Alpha-2 agonists were related to lower pain scores than midazolam in both verbal and visual scales ( $P < 0.05$ ). Our results correspond to the results of Schmidt *et al.* and children pre medicated with midazolam required more doses of rescue analgesic ( $P = 0.0015$ ).

Shukry *et al.*<sup>8</sup> found that there was reduced incidence of emergence delirium in children after sevoflurane-based general anesthesia.

Tobias<sup>9</sup> highlighted the role of dexmedetomidine in pediatric critical care and a pediatric anesthesia.

Ibacache *et al.*<sup>10</sup> stated that a single-dose dexmedetomidine reduces agitation after sevoflurane anesthesia in children.

In our study also, there is reduced incidence of post-operative agitation after sevoflurane anesthesia in children belonging to dexmedetomidine group.

It has been suggested that alpha-2 agonists prevent emergence agitation by reducing noradrenergic output from the locus coeruleus thus allowing increased firing of inhibitory systems such as the c-aminobutyric acid system.<sup>9</sup>

Blaine Easley *et al.*<sup>11</sup> studied on the effect of dexmedetomidine on post anesthesia shivering in children and concluded that dexmedetomidine was very effective in controlling it. Dexmedetomidine is an effective alternative in the treatment of already established post-operative shivering in children. In our study also, post-operative shivering was significantly less in children belonging to D Group (dexmedetomidine group), compared to children belonging to M Group (midazolam group).

Dodd-o *et al.*<sup>12</sup> in their study opined that the ability of alpha-2 agonists to decrease sympathetic nervous system activity without paralysis of compensatory homeostatic reflexes was highly desirable in pediatric anesthesia.

In our study also dexmedetomidine decreased sympathetic activity and produced desirable hypotension and bradycardia, when compared to Midazolam.

Zub *et al.*<sup>13</sup> found that oral route of administration of dexmedetomidine was a better alternative to IV route of administration.

Studies by Kanegaye *et al.*<sup>14</sup> and Breschan *et al.*<sup>15</sup> also failed to show a reduction in emergence agitation after midazolam premedication.

We also feel that oral administration of dexmedetomidine may be a viable alternative to IV administration and merits further investigation.

## CONCLUSION

Based on this study, we conclude that dexmedetomidine may be an effective oral premedicant prior to anesthesia-induction in children compared to oral midazolam, as it resulted in significantly lower post-operative pain, decreased post-operative agitation, less incidence of post-operative shivering, as well as more hemodynamic stability.

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# Safety and Efficacy of Combined Cervical and Interscalene Block for Clavicular Plating Surgery: A Prospective Clinical Study

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## Abstract

**Introduction:** Patients with clavicular fractures are usually done under general anesthesia for the plating surgery. Patients with high-risk factors for general anesthesia such as chronic obstructive pulmonary disease, ischemic heart disease, associated rib fractures, pneumothorax, and hemothorax have high risk for surgery. In order to decrease the risk for surgery, we evaluated for an alternative technique of anesthesia for clavicular surgeries.

**Aims and Objectives:** The aim of this study was to evaluate safety and efficacy of combined cervical and inter-scalene block for clavicular plating and to assess its efficacy of providing surgical anesthesia, intraoperative complications and post-operative benefits and complications.

**Materials and Methods:** In the present study, 30 patients of age group between 20 and 70 years of age were taken. Ipsilateral cervical plexus both superficial and deep and intrascapular block was performed in all patients with local anesthetic solution of 40 ml of 0.5% ropivacaine. To allay anxiety, injection of 1 mg midazolam was given intravenously prior to block and intravenous butorphanol tartrate 2 mg was given before starting of surgery for Intraoperative analgesia. Only American Society of Anesthesiologists (ASA) 1, 2, 3 groups were selected. A total of 16 patients were ASA-1 group, 8 patients were ASA-2 group and 6 patients were ASA group 3.

**Results:** Forced vital capacity was measured before block, 10 min after combined block and in the recovery room. There was no significant difference between forced vital capacity signifying absences of phrenic nerve palsy. Post-operatively patients had no pain for a long period. Required lower dose of opioid analgesic and lower incidence of post-operative nausea and vomiting.

**Conclusions:** The study indicates that regional anesthesia is an appropriate alternative to general anesthesia in patients undergoing clavicular surgery and do not compromise respiratory function. The study highlights the advantage of regional anesthesia having low morbidity and mortality over general anesthesia in patients with high risk factors undergoing clavicle surgery.

**Keywords:** Cervical plexus block, Clavicle surgery, Interscalene block, Ropivacaine

## INTRODUCTION

Clavicle fractures are commonly associated with multiple rib fractures, pneumothorax and hemothorax. Clavicle surgeries done under general anesthesia with multiple rib fractures, pneumothorax and haemothorax, post-operative pain is significantly higher and augmented by fracture ribs pain and pneumothorax.

Previously, it has been proposed that local anesthetic injection solution into ipsilateral cervical plexus and

intrascapular area could easily lead to the establishment of block appropriate for clavicle surgery.<sup>1,2</sup> Combined block is associated with decreased need of opioids for controlling post-operative pain. It also decreases post-operative nausea and vomiting, post-operative pulmonary complications and finally intensive care unit (ICU) stay of the patient.

In the present study, efforts have been made to know the efficacy and safety of combined cervical and intrascapular block as an anesthetic procedure for clavicular surgeries (Figure 1).



**Figure 1: (a-d) Intraoperative photos of clavicular surgery under combined cervical and interscalene block**

## MATERIALS AND METHODS

The present study was conducted at Department of Anesthesiology Government Medical College, Ananthapuramu. Ethical clearance was obtained from institutional Ethics Committee. 30 patients who provided written consent of American Society of Anesthesiologists (ASA) Status 1, 2, 3 of age group between 20 and 70 years were enrolled in this clinical study. Patients who didn't want to participate, with age <20 years and age >70 years, ASA status of 4 and 5, bleeding disorders, allergy to any of the study drug, chronic analgesic use and psychiatric diseases were excluded from the study.

Patients were thoroughly explained about the procedure during the pre-operative visit on the day before surgery. Also, they were informed about the risks and benefits associated with it. They were made well conversant with the visual analogue scale (VAS) for post-operative pain assessment. Patients were advised to be on fasting before the operative procedure for a period of 6 h and premedication with tablet diazepam 10 mg was given the night before surgery.

On arrival to the operation theater (OT) complex patients were taken to OT, where combined cervical and interscalene was performed. Intravenous (IV) infusion of 5% dextrose solution as maintenance fluid was started. All necessary equipment required for general anesthesia is kept ready in case of combined block failure and nerve block complications. Baseline parameters like pulse rate, noninvasive blood pressure (NIBP), respiratory rate, etc., were noted. Time for giving block and time for the onset of block and surgical anesthesia were noted. Monitoring was continuously done throughout the procedures.

Patient was given dose of midazolam 1 mg IV in the OT before the block placement to decrease anxiety and discomfort during the procedure while maintaining meaningful patient contact. Butorphanol tartrate 2 mg IV was given as intraoperative analgesic drug. 40 ml of 0.5% ropivacaine was used as a local anesthetic drug for combined block.

Under aseptic precautions cervical plexus both superficial and deep plexus block, interscalene block was achieved.<sup>3</sup>

Superficial cervical plexus block achieved by keeping the patient in the supine position, small towel kept under the patient head and head turned towards the opposite side. Midpoint of the posterior border of the Sternocleidomastoid is identified, usually the point lies where external jugular vein crosses the sternocleidomastoid muscle. A 22 g 5 cm needle is advanced 1-2 inches superior and inferior into sub-fascia along the posterior border of Sternocleidomastoid muscle and 5 ml of 0.5% ropivacaine is injected after negative aspiration. Paresthesia is usually not elicited.

Deep cervical plexus achieved by keeping the patient in the supine position, small towel kept under the patient head, and head turned towards the opposite side. Mastoid process is identified, line drawn from the tip of the mastoid process to transverse the process of C6 vertebra (chassaignac's tubercle), to confirm C6 transverse process a line is drawn posteriorly from the cricoid cartilage to intersect the line from the mastoid process. Another line is drawn 1 cm posterior to the vertical line. C2 transverse process lies 1.5 cm below the mastoid process in the second vertical line. C3 transverse lies 1.5 cm below C2 and C4 lies 1.5 cm below C3. C4 transverse process is confirmed by a horizontal line drawn from the lower border of the mandible to the second vertical line 22 g 5 cm needle is inserted towards C2 transverse process, after getting contact with the transverse process elicit paresthesia by walking on the transverse process and after negative aspiration for blood and cerebrospinal fluid 5 ml of 0.5% ropivacaine is injected. Repeat the procedure at C3 and C4 levels.

Interscalene block<sup>4</sup> is achieved by keeping the patient in the supine position, and head turned toward the opposite side. Interscalenous groove is identified, which lies immediately behind the lateral border of the clavicular head of the sternocleidomastoid muscle at the level of cricoid cartilage. Prominent tubercle present on the C6 transverse process chassaignac's tubercle is identified. Interscalenous groove is palpated by rolling the fingers posteriorly off the lateral border of the sternocleidomastoid muscle; mark the groove as high as possible 22 g, 2.5 cm needle is introduced and

directed medially, caudally, and slight posteriorly in the direction of the C6 transverse process. Paresthesia is elicited, and 20 ml of 0.5% ropivacaine is injected.

Strict vigilance is kept for the complications of the cervical plexus and interscalenous block like intravascular injury,<sup>5</sup> injection into the vertebral artery, loss of consciousness, seizures, temporary partial phrenic block, central nervous system (CNS) toxicity (tinnitus, disorientation, perioral numbness, cardiovascular collapse,<sup>6</sup> recurrent laryngeal nerve blockade, hoarseness of voice, Horner's syndrome (ptosis, miosis, anhydrosis), vagal nerve blockade, epidural/subarachnoid (total spinal), hematoma.

Patients were monitored with multichannel monitor for SPO<sub>2</sub>, pulse rate, NIBP, respiratory rate, temperature, 6 lead electrocardiography, induction time (time for surgical anesthesia) was defined as the time gap between the completion of local anesthetic injection to pinprick discrimination. Recovery time was defined as the time between applications of bandage to eye opening on verbal command.

Post-operatively all the patients were shifted to the recovery room ICU for first 24 h. Patients were assessed for pain nausea and vomiting just after shifting to the recovery room ICU.

Data were collected at 2, 4, 6, 8, 10, 12 and 24 h respectively and calculated from the time of block. Post-operative pain assessed with VAS score of 0-10 (0 = no pain, 10 = worst imaginable pain). VAS scores >4 were treated with butorphanol tartrate 1 mg IV, repeated if necessary after 15 min. If analgesia is still inadequate after 30 min injection diclofenac sodium 75 mg intramuscular administered as back up the analgesic. The total administered doses of butorphanol tartrate and diclofenac sodium during the first 24 h was recorded. Time for the first-analgesic requirement was noted. Duration of post-operative analgesia was defined as the time between last suture application and requirement for first-rescue analgesic at VAS score above 4.

Patients were monitored throughout the study period for evidence of feeling of pain during surgery, cough and acceptance of the procedure. The surgeon assesses the quality of anesthesia following numeric ranking scale (NRS) OF 0-100. At the time of discharge, patients were asked to mention about the satisfaction of the respective procedure NRS OF 0-100.

## RESULTS

The study was conducted over 24 month period. All the patients tolerated the procedure well under combined

cervical plexus and intrascalenous block, except for 3 patients who required small supplemental doses of propofol 100 mg during surgery. The mean duration of surgery was 78 ± 22.98 min. The patients were comfortably maintained with sedation during the procedure with no untoward effect.

We have not observed any incidence of direct epidural/subarachnoid spread, inadvertent intravascular injection, and hemodynamic instability, persistent pain after block, CNS toxicity, phrenic nerve palsy, recurrent laryngeal nerve palsy, vagal nerve blockade and hematoma.<sup>7</sup> Two patients had Horner's syndrome (ptosis, miosis and anhydrosis) temporarily and recovered completely after 6 h. Three patients required injection diclofenac sodium 75 mg as back up the analgesic. Demographic and pre-operative parameters are represented in Table 1, intraoperative characteristics in Table 2, post-operative analgesia and post-operative nausea and vomiting in Table 3, incidence of complications of the cervical plexus and interscalenous in Table 4.

## DISCUSSION

Regional anesthesia using cervical plexus and interscalenous have been used as an ideal alternative to general anesthesia for selected patients undergoing clavicle surgeries.<sup>8</sup> Low

**Table 1: Demographic and pre-operative parameters**

Parameters	Value
Age (years)	41.3±13.68
Weight (kg)	51.87±5.32
Height (cm)	154.97±4.33
BMI (kg/m <sup>2</sup> )	21.27±0.02
ASA status (I/II/III)	I - 16/30 II - 8/30 III - 6/30
Pre-operative pulse (BPM)	77.33±7.35
Pre-operative MAP (mmHg)	92±8.35
Pre-operative SPO <sub>2</sub> (%)	99.1±0.75

Data are given as mean±SD, except ASA physical status. BPM: Beats per minute, BMI: Body mass index, MAP: Mean arterial pressure, ASA: American Society of Anesthesiologists, SD: Standard deviation

**Table 2: Intraoperative characteristics**

Parameters	Value
Induction time (min)	14.20±1.6
Duration of surgery (min)	78.72±22.98
Recovery time (min)	2.51±0.68
Total OT time (min)	94.28±19.74
Intraoperative pulse (BPM)	77.11±7.05
Intraoperative MAP (mmHg)	89.93±7.68
Intraoperative SPO <sub>2</sub> (%)	99.05±0.83
Surgeon satisfaction score (0-100)	78.67±8.50

Data are given as mean±SD. BPM: Beats per minute, MAP: Mean arterial pressure, SD: Standard deviation, OT: Operation theater



**Table 3: Post-operative analgesia and PONV**

Parameters	Value
Time to first analgesic at VAS $\geq$ 4 (min)	388 $\pm$ 46.4
Total butorphanol (mg)	4.51 $\pm$ 0.78
Patient diclofenac receiving (%)	3 (10)
VAS score in immediate post-operative period	1.03 $\pm$ 0.88
VAS score at 2 h	0
VAS score at 4 h	1.86 $\pm$ 0.34
VAS score at 6 h	3.78 $\pm$ 0.74
VAS score at 12 h	2.58 $\pm$ 0.72
VAS score at 24 h	2.43 $\pm$ 0.50
VAS score at first rescue analgesic administration	4.67 $\pm$ 0.88
Maximum VAS score in 24 h	4.67 $\pm$ 0.88
PONV requiring treatment (%)	5 (16.6)
Patient satisfaction score (0-100)	80.69 $\pm$ 9.13

Data are given as mean $\pm$ SD, PONV: Post-operative nausea and vomiting, VAS: Visual analogue scale, SD: Standard deviation

**Table 4: Incidence of complication of bilateral cervical plexus block**

Parameters	Value
Intravascular injection/injury	0
Vertebral artery	0
Phrenic nerve block	0
CNS toxicity	0
Cardiovascular collapse	0
Recurrent laryngeal nerve blockade	0
Horner's syndrome (transient) (%)	2 (6.66)
Vagal nerve block	0
Epidural/subarachnoid/(total spinal)	0

CNS: Central nervous system

concentration of local anesthetic drug 0.5% ropivacaine is used for clavicle surgery because not much muscular relaxation is needed for clavicle surgery, only sensory blockade is sufficient. Low concentration and higher volume of local anesthetic drug have higher success rate of block than high concentration and low volume of drug. Low concentration and higher volume local anesthetic drug have lesser systemic toxicity than high concentration and low volume drug in case of accidental intravascular injection and epidural/subarachnoid spread. Benefits include prolonged post-operative pain relief,<sup>9</sup> reduction in dosage of use opioids in post-operative period, reduction in post-operative nausea and vomiting, reduced ICU stay, reduced post-operative pulmonary complications and potential for early ambulation.

The means to assess post-operative pain control was the time to first analgesic request minutes, total amount of analgesic consumed in the first 24 h period after surgery butorphanol 4.51  $\pm$  0.78 mg and the VAS scores at different times in the first post-operative day.

Patients had prolonged post-operative pain relief, lower consumption of butorphanol 4.51  $\pm$  0.78 mg in the first 24 h after surgery.<sup>10</sup> Only 3 patients required inj. Diclofenac

sodium 75 mg as back up analgesic in the first 24 h after surgery. We had higher surgeon satisfaction scores and patient's satisfaction scores 78.67  $\pm$  8.50 and 80.69  $\pm$  9.13.<sup>11</sup> There was no significant difference in forced vital capacity before surgery, 10 min after block and in the immediate post-operative period signifying absence of phrenic nerve palsy.

Major complications were not encountered in our study expect for incidence of Horner's syndrome temporarily in 2 patients which recovered completely after 6 h. To conclude in view of excellent analgesia in the early post-operative period<sup>12</sup> requirement of significantly lesser amount of post-operative analgesics, decrease in the occurrence of post-operative nausea and vomiting and low rate of serious complications, along with potential for early ambulation and home discharge. Combined cervical plexus and interscalene block<sup>13</sup> can be used as a suitable alternative to general anesthesia as the anesthetic procedure in clavicle surgery. Probability of inconsistent block, high technical difficulty in performing the block by inexperienced hands and high incidence of serious major complications in inexperienced hands limits its use as conventional anesthetic technique for clavicle surgeries.

## CONCLUSION

Combined cervical plexus and interscalenous block is safe and effective anesthetic technique in experienced hands for clavicular surgeries in selected group of patients where high risk factors for general anesthesia are present,<sup>14</sup> without any compromise in respiratory function of the patient.

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# Prevalence of Refractive Errors among School Children in Jaipur, Rajasthan

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## Abstract

**Introduction:** Children's proper vision is essential for successful learning in school. When the vision suffers, child's routine schoolwork and day-to-day activities also get affected.

**Aims and Objective:** The present study was conducted to determine the prevalence of refractive errors in urban school going children of Jaipur, Rajasthan, the frequency of the various types of refractory error, and their relationship to sexuality and to know the percentage of students who wore glasses.

**Materials and Methods:** A school-based cross-sectional descriptive study was done in schools of Jaipur. Randomly selected students from schools of Jaipur, Rajasthan were taken as samples for this study. Screening was done at the respective classroom under the supervision of the class teacher. A total of 928 students were screened. Of which 464 were girls (232 aged 5-12 years, 232 aged 13-18 years) and 464 were boys (232 aged 5-12, 232 aged 13-18). The names and address of the students who were having vision equal to or <6/9 were noted and were called at Mahatma Gandhi medical College and Hospital in the ophthalmology department for confirmation by detailed examination.

**Results:** Prevalence of refractory error was 30.39%. Myopia was most common (63.47%) type of refractory error, followed by astigmatism (25.18%), and followed by hypermetropia (11.35%). Girls (53.91%) were affected more than boys (46.09%). Only (67.03%) were diagnosed earlier other (32.97%) were diagnosed for the first time. Among them, only (66.67%) were wearing spectacles at the time of visit.

**Conclusion:** There is a need to have regular and simple vision testing in school children so as to detect those who may suffer from these disabilities. The possible reason for students for not wearing glasses may be a lack of awareness about refractive error. However, some of them quote it as shame or shy to wear eyeglasses, especially girls. School screening should be made mandatory by the government health authorities.

**Keywords:** Astigmatism, Hypermetropia, Myopia, Refractive error

## INTRODUCTION

Child's vision is essential for successful learning in school. When the vision suffers, child's routine schoolwork and day to day activities also get affected.<sup>1</sup> Vision problems are common among school going children's. Children who have been affected could not concentrate on studies or any other curricular or extracurricular or recreational activities.

In normal individuals, parallel rays passing the eye are focused on the retina to form a circle of least diffusion. Such a state of refraction is termed as emmetropia. The far point is at infinity. If in a state of rest of the eye the

parallel rays are not focused on the retina and do not form a circle of least diffusion, the eye is said to be in an ametropic state.<sup>2</sup> If the rays are brought to a focus behind the retina the error is hypermetropic due to lesser refractive power of the eye, and if the rays are focused in front of the retina, the error is myopic due to more refractive power of the eye. When the rays of light from more than one meridian are brought to a focus at different points. i.e. the refractive system is not concentric and no single focus is formed, the eye is in a state of refraction, which is termed astigmatism.

Refractory error remains one of the primary causes of visual impairment in children worldwide.<sup>3</sup> Refractive error

is the simplest and safest to treat the major vision problems. Yet uncorrected and under-corrected refractive error remains the most common cause of poor vision among children. To address the issue of blindness in children, the WHO recently launched a global initiative, VISION 2020 – The right to sight, to eliminate avoidable blindness among children.<sup>4</sup> Despite the fact that it is such a serious problem only a few papers as the prevalence of refractory error among school children in India have been published so far. Having this in mind we decided to study more closely the prevalence of refractory error in school children.

School screening programs have been an established part of the school health services and remain universally recommended. These programs are primarily aimed at detecting refractory errors. Schools are also one of the best centers for effectively implementing the comprehensive eye healthcare programme.<sup>5</sup>

## MATERIALS AND METHODS

Randomly selected students from schools of Jaipur, Rajasthan were taken as samples for this study. Formal permission was taken from the principal of the school. Screening was done at the respective classroom under the supervision of the class teacher. A total of 928 students, 464 girls (232 aged 5-12 years, 232 aged 13-18 years), 464 boys (232 aged 5-12, 232 aged 13-18) were screened. Visual acuity was tested by Snellen's chart for distant vision keeping it at 6 meters from the subjects, and near vision was tested with the help of Jaeger's chart keeping at a distance at 25-30 cm. The names and address of the students who were having vision  $\leq 6/9$  were noted and were called at Mahatma Gandhi Medical College and Hospital in the ophthalmology department for confirmation by detailed examination. In ophthalmology department dry and wet retinoscopy, slit lamp examination, fundus examination and best corrected visual acuity (subjective refraction) was determined. The refractory error was expressed as the spherical equivalent (SE). Myopia was defined as SE of at least  $-0.50D$ , hypermetropia as SE of at least  $+0.50D$ , astigmatism was diagnosed when the difference in the refraction of axes in one eye was  $<0.50DC$ .

However, in this study we did not consider the predictors of refractory error (myopia) as reported in several studies. These include socioeconomic status, parent's education, and hereditary factors. The data presented here pertains only to decreased visual acuity due to refractive errors, which improved with the prescription of proper spectacles. Children with corneal opacities, retinal pathology, strabismus and amblyopia (though encountered in very few children) were excluded from this study.

## RESULTS

Prevalence of refractory error was 30.39%. Myopia was most common (63.47%) type of refractory error, followed by astigmatism (25.18%), and followed by hypermetropia (11.35%). Girls (53.91%) were affected more than boys (46.09%). Only (67.03%) were diagnosed earlier other (32.97%) were diagnosed for the first time. Among them, only (66.67%) were wearing spectacles at the time of visit.

## DISCUSSION

In our present study, there were 928 students in the 5-18 year age group. The number of students who had decreased vision (defined as visual acuity equal to or  $<6/9$ ) was 282. In our study prevalence of refractory error is 30.39% (Table 1).

It is quite high when compared to a study conducted by Jha<sup>6</sup> in Leh, Jammu and Kashmir, India and they found that the prevalence of refractive error was 5.69% and study conducted by Niroula and Saha<sup>7</sup> from Nepal in which they found that the prevalence of refractive error was 6.43% i.e. 62 schools children out of 964.

Almost similar prevalence was observed in the study conducted by Sethi and Kathra<sup>8</sup> in their study they found that the refractive error was 25.32% of the school children.

In another study by Singh<sup>9</sup> in Bhopal Madhya Pradesh, found that of the total 3016 students examined refractory error was 47.91%.

In our study, we observe out of 282 children's who had decreased vision, 179 (63.47%) were myopes, 71 (25.18%) had astigmatism, and 32 (11.35%) had hypermetropia (Table 2).

A study conducted by Kawuma and Mayeku<sup>10</sup> in Kampala district they found that the commonest refractive error was astigmatism with 38 (52%) children, followed by hypermetropia with 27 (37%) children, and myopia with 8 (11%) children.

In a study of prevalence of refractive errors in school children of Tafila city conducted by Hussein and Ahmed<sup>11</sup>

**Table 1: Prevalence of refractive error**

Variables	Number	Percentage
Present	282	30.39
Absent	646	69.61
Total	928	100



they found that myopia (63.5%) was the most common type of refractive errors followed by hypermetropia 11.2% and astigmatism 20.4%.

A study by Matta, *et al.*<sup>12</sup> In their study, they found that out of 124 children with refractive error, 55.6% had myopia, hypermetropia was seen in 16.9% and astigmatism was prevalent in 27.4% of children.

In our study, we observe that the number of girls 152 out of 282 (53.91%) with decreased visual acuity is higher as compared to boys 130 out of 282 (46.09%). The results were similar to study done by Sharma *et al.*<sup>13</sup> in their study conducted in rural blocks of Haryana they found that prevalence of refractive error was 23.7% in girls and only 12.2% in boys (Table 3).

The more number of female affected than male was found in many other studies though prevalence varies from the present study. Although, association between gender and refractive error was not found, but this high prevalence in female might be due to the higher rate of growth in girls and also because girls attain puberty earlier than boys.

In our study, we observed that 189 out of 282 (67.03%) were already diagnosed of refractory error but still 93 out of 282 (32.97%) were diagnosed for the first time of decreased vision and having refractory error (Table 4).

In a study done by Kumar *et al.*<sup>14</sup> out of the total 72 students with refractory error 12 (16.67%) were already diagnosed, whereas 60 (83.33%) remained undiagnosed till the study.

We feel that the percentage can be quite high in lower socio-economic status and in a rural school going children's. It will be interesting to study the results of rural school going children. Therefore screening in school going children should be carried out periodically as they constitute a particularly vulnerable group where uncorrected refractory error may have a dramatic impact on learning capability and education potential.

In our study, we observe that 33.33% children were not wearing spectacle at the time of visit after already being diagnosed of refractory error. In a study done by Kumar *et al.*<sup>14</sup> 66.67% children were not wearing spectacle at the time of visit (Table 5).

A possible reason may be a lack of awareness or shy to wear glasses. Therefore, we feel counseling of children and more importantly their parents is of equal and utmost importance as that of diagnosing and prescribing glasses which is mostly not done by busy ophthalmologist.

**Table 2: Distribution of students according to types of refractive errors**

Variables	Number	Percentage
Myopia	179	63.47
Astigmatism	71	25.18
Hypermetropia	32	11.35
Total	282	100

**Table 3: Distribution of students with refractory error according to gender**

Variables	Number	Percentage
Girls	152	53.91
Boys	130	46.09
Total	282	100

**Table 4: Distribution of students according to refractive error diagnosed or not diagnosed**

Variables	Number	Percentage
Already diagnosed	189	67.03
Not diagnosed before	93	32.97
Total	282	100

**Table 5: Compliance among school children who have spectacles**

Variables	Number	Percentage
Wearing spectacles at the time of visit	126	66.67
Not wearing spectacles at the time of visit	63	33.33
Total	189	100

## CONCLUSION

There is a need to have regular and simple vision testing in school children so as to detect those who may suffer from these disabilities. The possible reason for students for not wearing glasses may be a lack of awareness about refractive error. However, some of them quote it as shame or shy to wear eye glasses, especially girls. School screening should be made mandatory by the government health authorities.

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# Histopathological Evaluation of Masses of Nasal Cavity Region

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## Abstract

**Background:** A variety of malignant and benign conditions involve the nasal cavity and other anatomically related areas, and these are very common lesions encountered in clinical practice. Majority of diseases affecting these structures are due, in major part, to many of the specialized tissues, each with its own structural aberrations that exist in this region.

**Objective:** To analysis cases presenting as a mass in nasal cavity region over a period of 1 year in Teerthankar Mahaveer Medical College, and Research Centre, Moradabad.

**Materials and Methods:** All the cases were carefully examined histopathologically, and it was found that the region was affected by a variety of non-neoplastic lesions. A provisional diagnosis was made after clinical evaluation and radiological assessment, but final diagnosis was made after histopathological examination. Non-neoplastic lesions constituted 60% of these cases.

**Results:** Among 30 cases, 18 were benign, and 12 were malignant. In the decreasing order of frequency lesions were - nasal polyp, rhinoscleroma, tuberculosis, mycotic infection, fibrous dysplasia, ossifying fibroma, nasal glioma, and nasopharynx were involved by a range of benign lesions.

**Conclusion:** We concluded the study with the outcome that nasal polyps were the commonest lesions in the nasal cavity region in population of Western UP region.

**Keywords:** Benign lesions, Malignant lesions, Nasal cavity, Nasopharynx, Paranasal sinuses

## INTRODUCTION

A variety of malignant and benign conditions involve the nasal cavity and other anatomically related areas, and these are very common lesions encountered in clinical practice.

Pathologic basis of these lesions has always been a matter of contention.<sup>1</sup> In Majority of diseases affecting these structures is due, in major part, to many of the specialized tissues, each with its own structural aberrations that exist in this region. Such types of lesions mainly encountered in tropical countries.<sup>2</sup> Histo-pathological examination is the mainstay of final definitive diagnosis. Thus, a careful histological workup is essential for a correct diagnosis and timely intervention. The aim of this clinic-pathological study was to find out the incidence of benign and malignant

polypoidal lesions of the nasal cavity, para-nasal air sinuses and naso-pharyngeal region.

## MATERIALS AND METHODS

The study was conducted in the Departments of Pathology and ENT at Teerthankar Mahaveer Medical College, and Research Centre, Moradabad over a period of 1 year. The formalin-fixed specimens were received with complete clinical and radiological features. Routine gross examination and required number of sections were taken and stained with hematoxylin and eosin. Periodic acid Schiff's and other stains were used wherever necessary. Ethical and Institutional Research Committee approval was taken prior to conduct the study.

## RESULTS

A total 30 cases presented as a mass in nasal cavity region. Histological examination revealed that the benign lesions outnumbered the malignant lesions in the ratio of 1.5:1. The age of presentation ranged from 11 to 54 years of life. The mean age of presentation was 23.4 years, thus, indicating that the majority of the patients were young adults, and lesions of the nasal cavity and associated regions like paranasal air sinuses and nasopharynx had a stronger association for male gender when compared to females. Nasal cavity was the predominant site of involvement (74.48%) and peripheral nervous system (25.5%). No benign lesion was found in nasopharynx. However, a variety of benign and malignant tumors involved this region. Nasal polyp was the commonest lesion observed in this region. It constituted 80.16% of all benign cases. The other benign lesions in the decreasing order of frequency were - scleroma of the nose (rhinoscleroma) (4.83%), tuberculosis (4.04%), mycotic infections (3.45%), fibrous dysplasia, ossifying fibroma and cysts with two cases (1.28%) each, (0.63%) each of nasal glioma and ossifying fibroma was seen. Polyps of the nose were bilateral in 59% cases and presented as a mass in single nostril in the rest. Microscopically, the polyps were composed of loose mucus glands, covered by the epithelium of the concerned region the epithelium in some areas changed from one functional type to another (squamous metaplasia). The stroma was mainly infiltrated by plasma and neutrophil cells. Sometimes necrosis was seen indicating infarction. The basement membrane underlying the surface mucosa was markedly thickened. Rhinoscleroma was the second most common benign lesion in this region. The peak age of presentation was 41 years. Microscopically, the predominant cells were histiocytes and plasma cells. Tuberculous lesions presented with 2:1 male-to-female ratio. Microscopically, the granulomas were poorly formed and non-necrotic. They were composed of Langhan's cells, epithelioid cells, and lymphocytes arranged in follicular pattern. Mycotic infections presented with a male-to-female ratio of 1.5:1 which on microscopy, showed inflammation ranging from negligible to a large number of neutrophils and histiocytes cells. The culture was positive on Sabouraud's medium, confirming the mycotic infection. Cysts on microscopy showed features of epidermal inclusion cyst. Nasal glioma showed astrocytic neuroglial cells interlaced with fibrous and vascular connective tissue that was covered with nasal mucosa.

## DISCUSSION

The incidence of benign lesions as seen in this study well correlates with the study of Dasgupta *et al.*<sup>3</sup> However the

incidence reported by Tondon *et al.*<sup>4</sup> does not correlates with our study. It is important to recognize the range of benign lesions in this region and to differentiate them from malignant lesions because of different medical management. Nasal polyps were the commonest polypoidal lesions. Nasal polyps in our study were to the extent of (82.06%) as compared to the observations by Tondon *et al.*<sup>4</sup> (64%) and Dasgupta *et al.*<sup>3</sup> (62.85%) (Figure 1). Other presentations, in terms of age presentation, gender variation, and clinical presentation were similar. Nasal polyps in the present study were bilateral in 60% of cases in our study, but according to Batsakis<sup>5</sup> it were showed 100%. Rhinoscleroma in our study (4.83%) was lower than that observed by Tondon *et al.*<sup>4</sup> (9% of all inflammatory lesions). In a study performed by Tondon *et al.*<sup>3</sup> peak age of presentation was noted (20-29 years) as compared to our observation. Sporadic cases of rhinoscleroma have been detected from America, and Africa.<sup>6</sup> In our study tuberculous lesions were also noted Waldman *et al.*<sup>7</sup> and Nayar *et al.*<sup>8</sup> totally denied tuberculous entity. This is perhaps due to a higher prevalence of tuberculosis in other parts of the world. We did not classify the fungus, the overall incidence of fungal infections was 3.48%, but according to Tondon *et al.*<sup>3</sup> the incidence of rhinosporidiosis was 24%. According to study conducted by Tsai *et al.*<sup>9</sup> fibrous dysplasia in the nasal cavity is rare, but in the present study we found (1.67%) cases involving maxilla. Microscopic features were consistent with Ruggieri *et al.*<sup>10</sup> and Tsai *et al.*<sup>9</sup> The rarity of this lesion is documented by Lawton *et al.*<sup>11</sup> and Choi *et al.*<sup>12</sup> According to Jayachandran and Meenakshi,<sup>13</sup> ossifying fibroma is a rare benign tumor of jaw, a type of fibro-osseous lesions. In our study, the lesion was seen in maxilla of a 12-year-old girl. The most prominent histological feature of this lesion was the presence of large, well-defined, calcified small spherical bodies. Wischniewski *et al.*<sup>14</sup> their study found glioma to be present in children below 8 years of age, but Rahbar *et al.*<sup>15</sup> found confronted with this. The clinical and histological picture as seen in this study, well correlated with the study of Chang and Leu.<sup>16</sup>

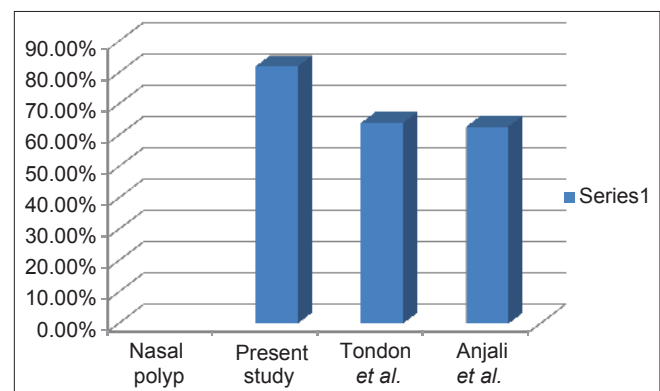


Figure 1: Incidence of nasal polyps in different studies



## CONCLUSION

The conclusion which we can draw from this study that in some observations our study correlates with the study of other researchers and on the hand contradicts with some other studies. The reason behind this seems to be different ethnic, geographical distribution and number of subjects on whom the study was conducted. In addition to this prior treatment taken by the patient before reaching to tertiary care level hospital.

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# Socio-economic Impact of Drug Abuse: A Hospital-Based Study

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## Abstract

**Background:** Drug abuse possesses problems not only on the individual users but also on the family and the community. Within the family, it is often the women who are most affected and bear a significant brunt of the burden.

**Materials and Methods:** This is a descriptive hospital-based study. After obtaining informed consent and satisfying inclusion-exclusion criteria, 30 subjects and their caretakers were included. International classification of diseases-10 criteria were used for the diagnosis. Family burden interview schedule was used to assess the family burden. Data were analyzed using appropriate statistical tests. The subjects were made into two groups, 15 with alcohol dependence and 15 with injecting drug use (IDU).

**Results:** The overall burden was higher on IDU than alcohol dependence. Spouses were generally more tolerant than the other caretakers. The value observed of subjective burden was lower in subjects of care-takers of the alcohol dependence syndrome (ADS), (46.7%) than that of care-takers of the IDUs (66.7%).

**Conclusion:** We concluded the study with the fact that more optimism is required by the spouse of the patient, and they should be more caring in cases of ADS and IDUs.

**Keywords:** Alcohol dependence syndrome, Caretakers, Drug abuse, Women

## INTRODUCTION

Drug abuse possesses problems not only on the individual users but also on the family and the community. Substance (drug) dependence syndrome is well-served in the literature by a wide variety of clinical, epidemiological, and laboratory studies, but the examination of its relationship to behavioral and environmental factors has gained importance only lately.<sup>1</sup> The costs that families incur in terms of economic hardships, social isolation, and psychological strain, are referred to as family burden.<sup>2</sup> The burden on families on account of substance abuse by a family member has begun to come into focus since the 1990s.<sup>3</sup>

Hoening and Hamilton in 1966 attempted to distinguish between objective and subjective burdens. The former includes the effects of the illness on finances and routine

of the family, while the latter is defined as the extent to which family members are affected by objective burden.<sup>4</sup>

Indeed drug abuse poses various kinds of problems impacting not just on the individual user, but also on the family and community in general. Within the family, it is often the woman, in the role of wife or mother who is most affected by the individual's substance use, and has to bear a significant part of the family burden. Such impact becomes even more obvious, where women are already disadvantaged. This aspect of the burden of substance use has received scant attention. Changing roles, increased stress, and alterations in lifestyle bring with them newer problems.<sup>5</sup>

Since families play a vital role in subject's support and treatment, this study may help in better understanding the problem and devising better prevention, coping, and treatment strategies.

## Aims

1. This study has been carried out to explore some important, but not yet explored aspects of substance dependence syndrome (SDS) i.e., the family burden perceived by the caretakers of these subjects.
2. The relevant clinico-socio-demographic profiles of the subjects, as well as those of the caretakers, were also studied.

## MATERIALS AND METHODS

The present study is a descriptive, hospital-based study in a 30 consecutive subjects fulfilling the diagnosis of “SDS” criteria according to the international classification of diseases-10.

The subjects were included from those attending the psychiatry outpatient department and admitted in the de-addiction ward or subjects referred from any other Departments of Teerthanker Mahaveer Medical College and Research Centre, Moradabad, India. The subjects were included by convenience sampling only after a consultant psychiatrist.

From the Department of Psychiatry independently confirmed the clinical diagnosis. The subjects were interviewed in one to one situation. In circumstances where the subjects were not ready for an immediate interview, then it was carried out as soon as the crisis was over. Written informed consent was taken from the subject, and the instruments were administered. The data were collected by applying the tools putting up with norms set by the original writer of the instruments. The data collection was the sole responsibility of the first author of this study.

## Tools

1. A clinico-socio-demographic proforma. This is a self-designed proforma. It was used for the collection of the relevant socio-demographic and clinical information required for the purpose of this study about the subjects and the caretaker
2. Family burden interview schedule. It is a semistructured interview schedule comprising 24 items grouped under six areas. Rating of burden is done on a three-point scale for each item and the standard question to assess the ‘subjective’ burden is also included in the schedule.<sup>3</sup> The source tool was translated to regional language by two translators using standard methodology.<sup>6</sup>

## Statistical Analysis

Frequencies and percentage were used to describe discrete variables. For the continuous data, mean values were calculated to measure the central tendencies whereas; range and standard deviation were computed to measure

dispersion. Chi-square test was utilized to test the significant association between discrete variables. *T*-test was used to test the significant difference between the continuous variables. The significance level was set at 0.5%.

## RESULTS

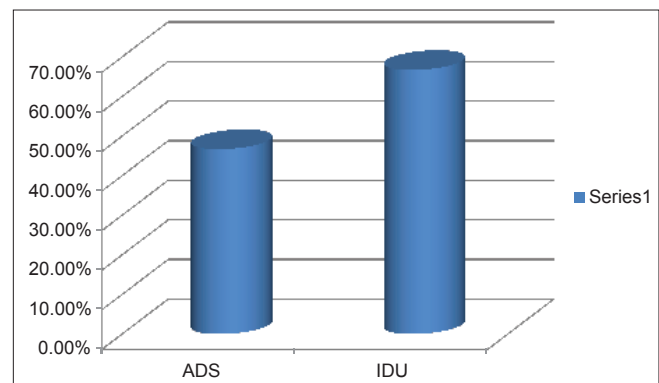
Thirty newly diagnosed cases and their caretakers were studied. Majority of the subjects were inpatients, undergoing detoxification. The subjects were divided into two groups: 15 with alcohol dependence syndrome (ADS) and 15 with injecting drug use (IDU) and hence, the interpretations in our study the overall subjective burden perceived by the care-taker of the subjects was  $1.73 \pm 0.45$ .

Among all care-takers, 73.3% had perceived severe burden. Subjective burden was higher in both the groups of subject 46.7% of care-takers of the ADS, 66.7% of care-takers of the IDUs reported severe burden (Figure 1).

## DISCUSSION

Our observations of the age at presentation of the SDS were in parallel to the majority of the studies conducted in other parts of India<sup>3,7</sup> and abroad.<sup>8-10</sup> The differences in the age at presentation can be explained in the light that the IDU, which is a socially, religiously and culturally unaccepted phenomenon, unlike drinking is expected to be detected by the family members and hence, present early in the treatment facilities. Moreover, IDU is likely to present to the treatment facilities earlier due to complications vis-à-vis ADS. In our study subjects, the majority were males. Our findings corroborates with other studies conducted outside India.<sup>3,10</sup>

Our findings contrasted the notion which consider a single person to be socio-cultural risk factors for substance dependence,<sup>11,12</sup> as the overall representations of the married subjects were more. Many other studies in India also found



**Figure 1: The difference in subjective burden perceived in alcohol dependence syndrome/injecting drug uses**

more subjects to be married.<sup>10,13</sup> This may be owing to the fact that due to lack of understanding of the problem, society stigma that marriage can solve the problems. Another reason for such findings in this study may be due to early marriages and cohesive marital bond. The higher rates of unemployment in points to the fact that many youngsters here have their father employed in the lower income jobs and away from the family. There is no job opportunity for them here and easily get into the unemployed peer groups. The fathers mostly live in distant places.<sup>14</sup> In contrast to the western studies where dependence is more common in broken homes, none of our subjects was from broken/disrupted families. But this finding was consistent in other studies conducted in India.<sup>10,14</sup> Unlike in the western studies which state in general that, IDU is associated with preexisting socio-economic deprivation, and most IDUs live in poverty belonging to low income households<sup>7</sup> more IDUs in our study belonged to higher income group. With these findings, we may say that early enquiry by the family members of the indiscretion on the part of the member of their family and early intervention may lessen the burden. In this study, the majority of the care-takers were married, and more than half of them were the spouses. It uncovers that almost half of the care-takers were housewives.

## CONCLUSION

The difference of subjective burden in both ADS and IDU may be due to the fact that alcohol use is a relatively accepted affair while IDUs is unambiguously perceived as devastating. Burden on all the problem areas was less on the spouse as compared to others. These findings in our study itself signify that the spouse may be more forbearing to the burden than the other family members. The study shows reason for some optimism to expand treatment of SDS as the families in general were found to be integrated, and the spouse in

particular was found to be caring. More treatment facilities and rehabilitation programs should be set up in the country.

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# Efficacy of Ultrasonography in the Management of Thyroid Swellings

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## Abstract

**Introduction:** Thyroid swelling is a common problem in clinical practice that poses challenges in detecting the type whether diffuse or nodular/solitary. Approximately, 7% of adults have palpable nodules, and 70% have nodule size <1 cm which are not palpable clinically, but visible on ultrasound. Hence, thyroid ultrasonography (USG) is safe, widely available, cost-effective investigation for diagnosis of thyroid swellings performed quickly and results interpreted readily.

**Aims and Objectives:** The aim was to determine whether the use of USG in patients with suspected thyroid swellings would change the diagnosis and management. In addition to, the study compared the intraoperative findings between clinical palpation and USG.

**Materials and Methods:** This was a comparative study conducted in 50 patients with thyroid swelling presented to the outpatient department between October 2006 and September 2008. The parameters included were age, sex, clinical and USG diagnosis, findings, and size, site and type of nodule.

**Results:** Clinically, out of 50 cases, there were 31 solitary nodular goiters (SNG), 7 multinodular goiters (MNG) and 12 diffuse goiters. USG revealed 17 SNG and 14 extra nodules out of 31 cases, 2 cases diagnosed as SNG from 7 MNG types and out of 12 diffuse goiters, 6 cases were SNG and 1 case was MNG. 7 cases that were suspected as malignant by ultrasound were confirmed in 3 cases on histopathological examination.

**Conclusions:** Clinical diagnosis confirmed by ultrasound in 25 patients out of 50 cases and indicated that ultrasound changes clinical diagnosis in 50% of the cases. The efficacy in detecting malignancy is still debatable.

**Keywords:** Diffuse goiter, Multinodular, Solitary nodular goiters, Thyroid swelling, Ultrasonography

## INTRODUCTION

High-resolution ultrasonography (USG) is the most sensitive imaging modality available for examination of the thyroid gland and associated abnormalities. Ultrasound scanning is non-invasive, widely available, less expensive, and does not use any ionizing radiation. Further, real-time ultrasound imaging helps to guide diagnostic and therapeutic interventional procedures in cases of thyroid disease. The major limitation of ultrasound in thyroid imaging is that it cannot determine thyroid function, i.e., whether the thyroid gland is underactive, overactive or normal in function; for which a blood test or radioactive isotope uptake test is required.<sup>1,2</sup>

Current USG technology permits high-resolution imaging of the thyroid gland that is more accurate than clinical palpation or other imaging techniques.<sup>3-5</sup> USG is safe and sensitive and is capable of detecting lesions as small as 1-3 mm in the thyroid parenchyma. Katz *et al.* reviewed the accuracy of thyroid USG in 28 thyroid glands examined the autopsy. The correlation between the USG finding of thyroid nodules and the pathologic finding of adenomatous goiter was good; USG thus had a sensitivity of 89% and a specificity of 84%.

The superiority of ultrasound examination of the thyroid over clinical examination has been described, with one study showing USG leading to a change in management

of 44% of patients who had been referred for a solitary nodule on physical examination. As has been eloquently described, “the ultrasound machine to the endocrinologist evaluating a thyroid nodule is analogous to the stethoscope of the cardiologist.”<sup>6</sup>

### Procedure of USG

The depth penetration and resolving power of ultrasound depend greatly on frequency. Depth penetration is inversely related, and spatial resolution is directly related to the frequency of the ultrasound. For the thyroid, a frequency of 7.5-10 or 14 MHz is generally optimal for all, but the largest goiters. Using these frequencies, nodules as small as 2-3 mm can be identified.

Routine protocols for sonography are not adequate. Although some technologists become extremely proficient after specific training and experience, supervision and participation by a knowledgeable and interested physician-sonographer is usually required to obtain a precise and pertinent answer to a specific problem that has been posed by the clinician. Standard sonographic reports may provide considerable information about the anatomy, but are suboptimal unless the specific clinical concern is explored and answered. Indeed, because some radiologists cannot address the clinical concern is explored and answered. Indeed, because some radiologists cannot address the clinical issue adequately, and for convenience, numerous thyroidologists perform their own ultrasound examinations, in which case it is essential that they have state-of-the-art equipment (that might not be cost-effective) and that they are willing to expand a considerable amount of time for a complete study.

Technical ingenuity, electronic enhancements such as Doppler capability, and even artistry are frequently required. Special maneuvers, various degrees of hyperextension of the neck, swallowing to facilitate elevation of the lower portions of the thyroid gland above the clavicles, swallowing water to identify the esophagus, and a valsalva maneuver to distend the jugular veins may enhance the value of data. Nevertheless, sonography is rather difficult to interpret the upper portion in of the jugular regions and in the areas adjacent to the trachea. Sonography is generally not useful below the clavicles.

## MATERIALS AND METHODS

The present study patients and clinical material was taken from JSS Hospital, Mysore. Data was collected in a pretested proforma, which meets the objective of the study. 50 cases were selected from the total number of cases by using purposive sampling method.

The analysis was performed using parameters, the descriptive statistics, Chi-square test.

### Inclusion Criteria

1. Patients with thyroid swelling
2. Patients above 16 years of age.

### Exclusion Criteria

1. All patients below 16 years of age
2. Patients with post-operative, recurrent thyroid swelling
3. Patients with systemic contraindications for surgery.

### Method of Study

1. To interview the patients and case history collection
2. Clinical examination of the thyroid swelling is done, and size of lobes, size of the nodule, number of nodule, site of nodule, type of nodule and clinical diagnosis is made
3. USG examination of the thyroid swelling is done, and size of lobes, size of the nodule, number of nodule, site of nodule, type of nodule and USG diagnosis is made
4. Other investigation like fine-needle aspiration cytology (FNAC), thyroid profile, blood investigations done. Systemic examination is done to rule out any contraindications for surgery
5. Surgery performed depending on ultrasound and FNAC findings. Operative diagnosis was made
6. Specimen sent for histopathological examination and the report collected latter.

### Statistical Methods Applied

#### Frequencies

The frequencies procedure provides statistics and graphical displays that are useful for describing many types of variables. The frequencies procedure is a good place to start looking at your data.

#### Descriptive

The descriptives procedure displays univariate summary statistics for several variables in a single table and calculates standardized values (z scores). Variables can be ordered by the size of their means (in ascending or descending order), alphabetically, or by the order in which you select the variables.

#### Chi-square

The Chi-square test procedure tabulates a variable into categories and computes a Chi-square statistic. This goodness-of-fit test compares the observed and expected frequencies in each category to test either that all categories contain the same proportion of values or that each category contains a user-specified proportion of values.

### Crosstabs

The crosstabs procedure forms two-way and multi-way tables and provides a variety of tests and measures of association for two-way tables. The structure of the table and whether categories are ordered determine what test or measure to use. SPSS for windows Version-16 (Inc Chicago 2007) was employed for statistical analysis.

## RESULTS

Most of the cases were in the age group of 31-40 years of age in both sex and least number of cases in age more than 60 years (Table 1, Graph 1).



**Figure 1:** Sonogram of the neck in the transverse plane showing a normal right thyroid lobe and isthmus. L: Small thyroid lobe in a patient who is taking suppressive amounts of L-thyroxine, I: Isthmus, T: Tracheal ring (dense white arc is calcification, distal to it is artifact), C: Carotid artery (note the enhanced echoes deep to the fluid-filled blood vessel), J: Jugular vein, S: Sternocleidomastoid muscle, M: Strap muscle



**Figure 2:** Sonogram of the left lobe of the thyroid gland in the transverse plane showing a rounded lobe of a goiter. L: Enlarged lobe, I: Widened isthmus, T: Trachea, C: Carotid artery (note the enhanced echoes deep to the fluid-filled blood vessel), S: Sternocleidomastoid muscle, M: Strap muscles, E: Esophagus

Most of the cases were females (about 90%) which are statistically significant (Table 2, Graph 2).

A significant association was observed between age and sex distribution, revealing pattern of distribution of scorer of cases was statistically different. Most of the cases were in the age group of 31-40 years of age in both sexes and least cases in age group more than 60 years (Table 3, Graph 3).

Mean ages of male and female were 46 and 38 respectively (Table 4).

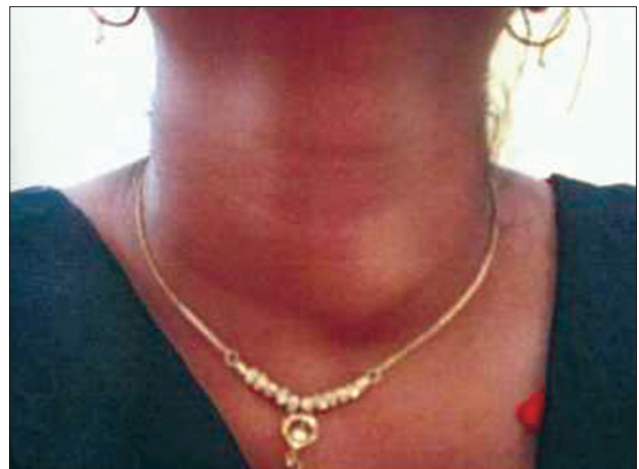
**Table 1: Age distribution of the cases**

Valid	Frequency	%	Valid (%)	Cumulative (%)
Below 30	14	28.0	28.0	28.0
31-40	17	34.0	34.0	62.0
41-50	13	26.0	26.0	88.0
51-60	5	10.0	10.0	98.0
60+	1	2.0	2.0	100.0
Total	50	100.0	100.0	

$P < 0.05$  is significant



**Figure 3:** Solitary thyroid nodule right side



**Figure 4:** Solitary thyroid nodule left side

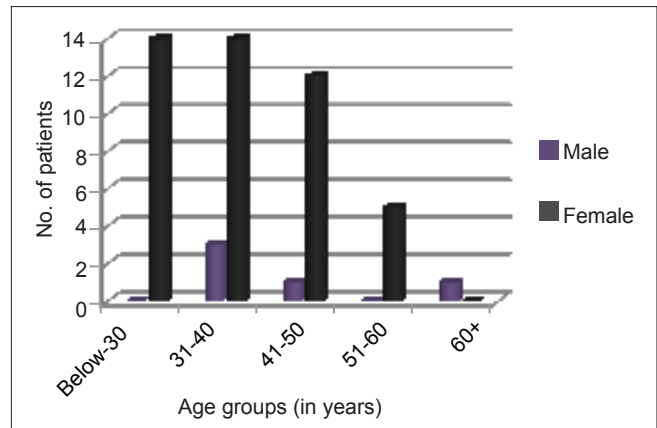
**Table 2: Sex distribution of the cases**

Valid	Frequency	%	Valid %	Cumulative %
Male	5	10.0	10.0	10.0
Female	45	90.0	90.0	100.0
Total	50	100.0	100.0	

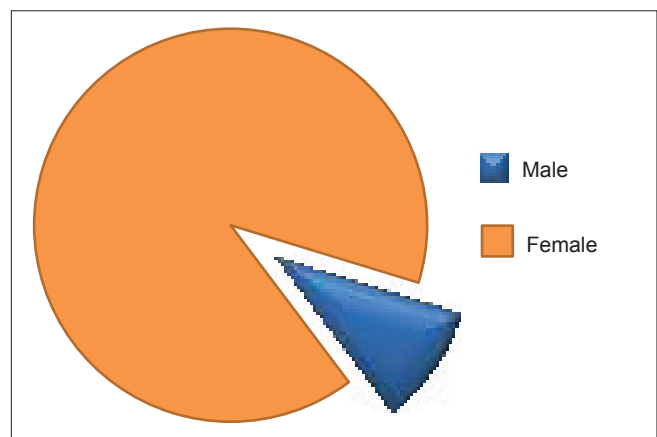
**Test statistic**

	Ages	Sex
Chi-square	18.000	32.000
Difference	4	1
Asymptotic significant	0.001	0.000

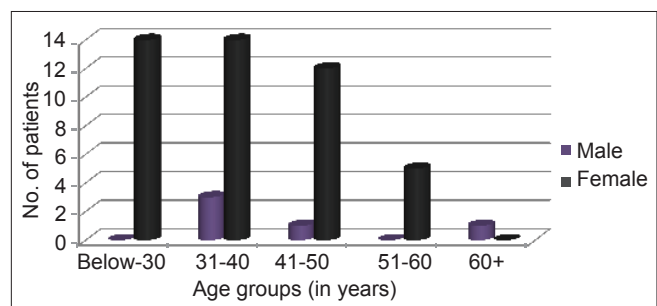
*P*<0.05 is significant

**Graph 1: Age distribution of the cases****Table 3: Age and sex co-relation**

Ages	Sex		Total
	Male	Female	
Below 30			
Count	0	14	14
% within sex	0	31.1	28.0
31-40			
Count	3	14	17
% within sex	60.0	31.1	34.0
41-50			
Count	1	12	13
% within sex	20.0	26.7	26.0
51-60			
Count	0	5	5
% within sex	0	11.1	10.0
60+			
Count	1	0	1
% within sex	20.0	0.0	2.0
Total			
Count	5	45	50
% within sex	100.0	100.0	100.0

**Graph 2: Sex distribution of the cases****Symmetric measures**

	Value	Approximate significant
Nominal by nominal Contingency coefficient	0.444	0.015
Number of valid cases	50	

**Graph 3: Age and sex co-relation****Table 4: The mean age and standard deviation (in years) according to sex**

	N	Mean	SD	Minimum	Maximum
Male	5	46.4000	17.28583	33.00	75.00
Female	45	38.1556	10.374770	20.00	60.00
Total	50	38.9800	11.28208	20.00	75.00

*P*<0.05 is significant, Mean ages of male and female were 46 and 38 respectively.  
SD: Standard deviation

A significant association was observed in left side thyroid lobe size between clinical examination and USG. Revealing pattern of distribution of scores of cases was statistically

different. 100% association was seen in 1, 2, and 5 cm nodules 90% with 3 cm nodule (Table 5, Graph 4).

A significant association was observed in right side thyroid lobe size between clinical examination and USG. Revealing pattern of distribution of scores of cases was statistically different. About 100% association was seen in 1 and 2 cm nodules (Table 6, Graph 5).

A significant association was observed for type of nodule between clinical examination and USG. Revealing pattern



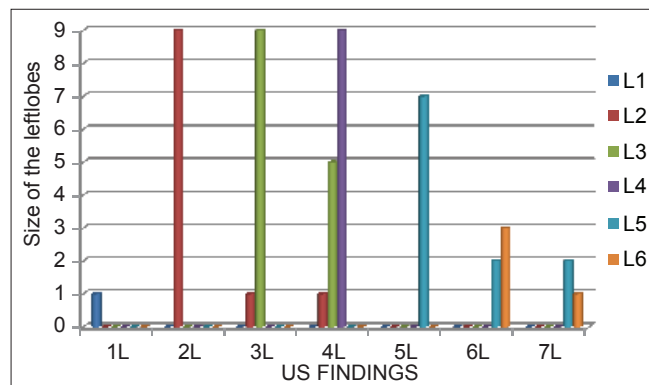
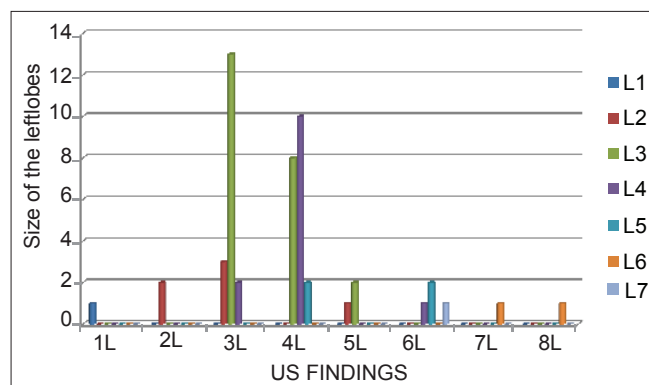
**Table 5: Comparison between size of left lobe of thyroid by clinical examination and USG**

SIZE L	USSIZE L							Total
	1.00	2.00	3.00	4.00	5.00	6.00	7.00	
1	1	0	0	0	0	0	0	1
	100.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0%
2	0	9	1	1	0	0	0	11
	0.0%	100.0%	10.0%	6.7%	0.0%	0.0%	0.0%	22%
3	0	0	9	5	0	0	0	14
	0.0%	0.0%	90.0%	33.3%	0.0%	0.0%	0.0%	28.08%
4	0	0	0	9	0	0	0	9
	0.0%	0.0%	0.0%	60.0%	0.0%	0.0%	0.0%	0.0%
5	0	0	0	0	7	2	2	11
	0.0%	0.0%	0.0%	0.0%	100.0%	40.0%	66.7%	22.0%
6	0	0	0	0	0	3	1	4
	0.0%	0.0%	0.0%	0.0%	0.0%	60.0%	33.3%	8.0%
Total	1	9	10	15	7	5	3	50
	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%

USG: Ultrasonography

**Symmetric measures**

		Value	Approximate significant
Nominal by nominal	Contingency coefficient	0.882	0.000
Number of valid cases		50	

 $P < 0.05$  is significant**Graph 4: Comparison between size of left lobe of thyroid by clinical examination and ultrasonography****Graph 5: Comparison between size of right lobe of thyroid by clinical examination and ultrasonography**

of distribution of scores of cases was statistically different. 95.7% association was seen in cystic and 66.7% in solid nodules (Table 7, Graph 6).

A significant association was observed between clinical diagnosis and USG diagnosis.

Revealing pattern of distribution of cases were statistically different (Table 8, Graph 7).

A significant association was observed between USG diagnosis and operative findings. Revealing pattern of distribution of scores of cases were statistically different. Where 100% matching was between solitary nodular goiters (SNG), multinodular goiters (MNG) and diffuse of USG diagnosis and operative findings (Table 9, Graph 8).

A significant association was observed for total number of nodule between clinical examination and USG. Revealing pattern of distribution of scores of cases were statistically different (Table 10, Graph 9).

A significant association was observed for total number of nodule between clinical examination and USG. Revealing pattern of distribution of scores of cases were statistically different (Table 11, Graph 10).

A significant association was observed for total number of nodule in right lobe of thyroid between clinical examination

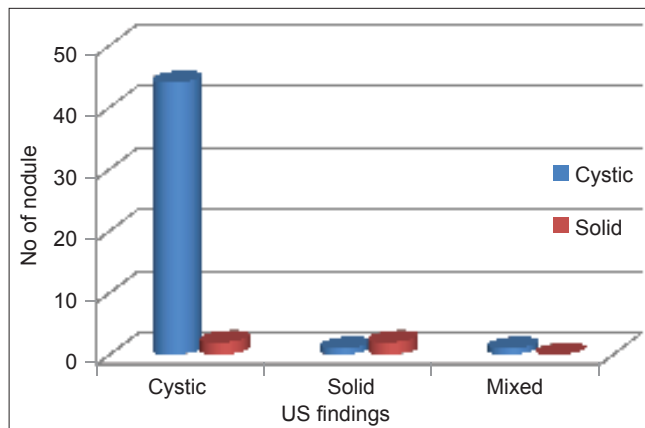
**Table 6: Comparison between size of right lobe of thyroid by clinical examination and USG**

SIZER	USSIZER								Total
	1.00	2.00	3.00	4.00	5.00	6.00	7.00	8.00	
1	1	0	0	0	0	0	0	0	1
	100.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	2%
2	0	2	3	0	1	0	0	0	6
	0.0%	100.0%	16.0%	6.7%	33%	0.0%	0.0%	0.0%	12.%
3	0	0	13	8	2	0	0	0	23
	0.0%	0.0%	72%	40%	66%	0%	0.0%	0.0%	46%
4	0	0	2	10	0	1	0	0	13
	0.0%	0.0%	11%	50%	0.0%	25%	0.0%	0.0%	26%
5	0	0	0	2	0	2	0	0	4
	0.0%	0.0%	0.0%	10%	0.0%	50%	0.0%	0.0%	8%
6	0	0	0	0	0	0	1	1	2
	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	100%	100%	4%
7	0	0	0	0	0	1	0	0	1
	0.0%	0.0%	0.0%	0.0%	0.0%	25%	0.0%	0.0%	2%
Total	1	2	18	20	3	4	1	1	50
	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%

USG: Ultrasonography

**Symmetric measures**

	Value	Approximate significant
Nominal by nominal Contingency coefficient	0.868	0.000
Number of valid cases	50	

*P*<0.05 is significant**Graph 6: Comparison between type of nodule by clinical examination and ultrasonography**

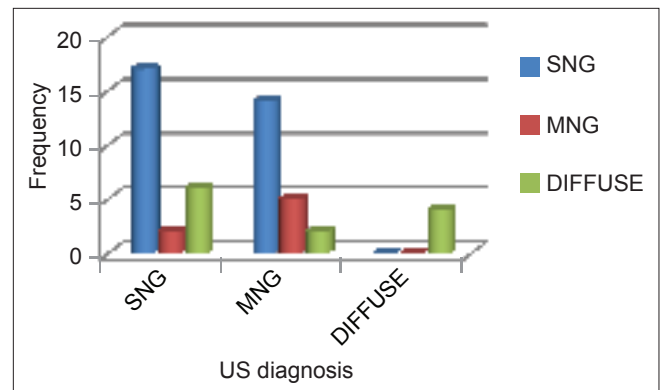
and USG. Revealing pattern of distribution of scores of cases were statistically different (Table 12, Graph 11).

**Surgery**

Sub-total thyroidectomy and hemithyroidectomy were the frequently performed surgeries (Table 13, Graph 12).

**DISCUSSION**

Out of the 50 cases studied, most of the cases (44 accounting for 88%) were in the age group of 20-50 years and only

**Graph 7: Comparison between clinical and ultrasonography diagnosis**

1 case accounting to 2% was seen in the age group of more than 60 years. The mean age among females was 38.1 with a standard deviation (SD) of 10 years and the mean age males was 46 years with a SD of 17 years. The minimum age was 20 years in females and 33 years in males and the maximum age were 60 years in female and 75 years in males. The mean age of all the cases together was 38, 9 years with SD of 11.2 years. 45 cases were females and 5 were males.

In our study, of the 50 cases compared between clinical examination and ultrasound, the size of thyroid lobe increased in 12 cases with respect to left lobe and 24 cases

**Table 7: Comparison between type of nodule by clinical examination and USG**

Type	Type	USTYPE		Total
	Cysti	Solid	Mixwd	
Cystic				
Count	44	1	1	46
% within USTYPE	95.7%	33.3%	100.0%	92.0%
Solid				
Count	2	2	0	4
% within USTYPE	4.3%	66.7%	0.0%	8.0%
Total				
Count	46	3	1	50
% within USTYPE	100.0%	100.0%	100.0%	100.0%

USG: Ultrasonography

**Symmetric measures**

		Value	Approximate significant
Nominal by nominal	Contingency coefficient	0.480	0.001
Number of valid cases		50	

*P*<0.05 is significant**Table 8: Comparison between clinical and USG diagnosis**

CLINI	USDIAGNO			Total
	SNG	MNG	Diffuse	
SNG	17	14	0	31
	68.0%	66.7%	0.0%	62.0%
MNG	2	5	0	7
	8.0%	23.8%	0.0%	14.0%
Diffuse	6	2	4	12
	24.0%	9.5%	100.0%	24.0%
Total	25	21	4	50
	100.0%	100.0%	100.0%	100.0%

SNG: Solitary nodular goiters, MNG: Multinodular goiters, USG: Ultrasonography

**Symmetric measures**

		Value	Approximate significant
Nominal by nominal	Contingency coefficient	0.502	0.002
Number of valid cases		50	

*P*<0.05 is significant

in the right lobe. Within 2 cm size of the lobe 3, the clinical examination was perfectly matching the ultrasound diagnosis. Increase in lobe size with ultrasound, was seen in cases above 3 cm lobes by clinical examinations.

Clinical examination revealed 46 cases were cystic, and 4 was solid type of nodule. Out of 46 cases of cystic, 1 was solid and 1 was mixed and out 4 solid, 2 were cystic and 2 were solid by USG examination.

31 cases were SNG, 7 were diffuse goiter out of 50 cases by clinical examination. 25 were SNG, 21 were MNG and

**Table 9: Comparison between ultrasound diagnosis and operative findings (cross tabs)**

USDIAGNO	OPEFIND			Total
	SNG	MNG	Diffuse	
SNG				
Count	25	0	0	25
% within opefind	100.0	0.0	0.0	50.0
MNG				
Count	0	21	0	21
% within opefind	0.0	100.0	0.0	42.0
Diffuse				
Count	0	0	4	4
% within opefind	0.0	0.0	100.0	8.0
Total				
Count	25	21	4	50
% within opefind	100.0	100.0	100.0	100.0

SNG: Solitary nodular goiters, MNG: Multinodular goiters

**Symmetric measures**

		Value	Approximate significant
Nominal by nominal	Contingency coefficient	0.816	0.000
Number of valid cases		50	

**Table 10: Comparison between total number of nodules by clinical examination and USG**

NODNO	USNOD					Total
	0	1	2	3	4	
0	4	6	1	0	1	12
	100.0%	20.0%	6.3%	0.0%	50.0%	20.0%
1	0	17	11	2	1	31
	0.0%	68.0%	68.8%	66.8%	50.0%	50.0%
2	0	2	4	1	0	7
	0.0%	8.0%	25.0%	33.3%	0.0%	10.04%
Total	4	25	16	3	2	50
	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%

USG: Ultrasonography

**Symmetric measures**

		Value	Approximate significant
Nominal by nominal	Contingency coefficient	0.529	0.013
Number of valid cases		50	

*P*<0.05 is significant

4 were diffuse goiter by USG, examination Ultrasound was able to identify extra nodule in 14 cases of 31 SNG by clinical palpation and in 7 MNG there was only 1 nodule was found by ultrasound in 2 cases and more than 1 nodule were found in 2 cases. In 24 cases out of 50, the diagnosis was changed and it accounts for about 48% of total cases. These results were comparable with the literature.

Thyroid nodules are a common problem. They are found in 4-8% of adults by palpation and in 13-67% when

**Table 11: Comparison between total number of nodules in left lobe by clinical examinations and USG**

NOL	USNOL			Total
	0.00	1.00	2.00	
0				
Count	18	12	1	31
% within opefind	94.7	42.9	33.3	62.0
1				
Count	1	15	1	17
% within opefind	5.3	53.6	33.3	34.0
2				
Count	0	1	1	2
% within opefind	0.0	3.6	33.3	4.0
Total				
Count	19	28	3	50
% within opefind	100.0	100.0	100.0	100.0

USG: Ultrasonography

**Symmetric measures**

		Value	Approximate significance
Nominal by nominal	Contingency coefficient	0.538	0.000
	Number of valid cases	50	

 $P < 0.05$  is significant**Table 12: Comparison between total number of nodules in right lobe by clinical examination and USG**

NOL	USNOL			Total
	0.00	1.00	2.00	
0				
Count	18	7	3	28
% within USNOR	100.0	29.2	37.5	56.0
1				
Count	0	17	4	21
% within USNOR	0.0	70.8	50.0	42.0
2				
Count	0	0	1	1
% within USNOR	0.0	0.0	12.5	2.0
Total				
Count	18	24	8	50
% within USNOR	100.0	100.0	100.0	100.0

USG: Ultrasonography

**Symmetric measures**

		Value	Approximate significance
Nominal by nominal	Contingency coefficient	0.596	0.000
	Number of valid cases	50	

 $P < 0.05$  is significant

ultrasound detection is used. In autopsy studies, they have a prevalence of approximately 50%.<sup>7,8</sup>

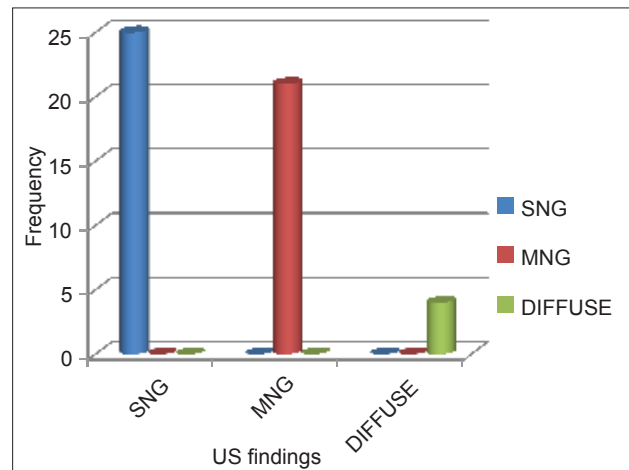
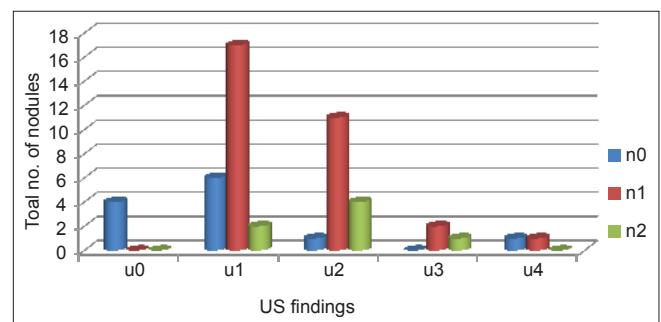
The superiority of ultrasound examination of the thyroid over clinical examination has been described, with one

**Table 13: The frequency of different surgeries**

Valid	Frequency	%	Valid %	Cumulative %
ST	24	48.0	48.0	48.0
HT	23	46.0	46.0	94.0
TT	3	6.0	6.0	100.0
Total	50	100.0	100.0	

**Test statistics**

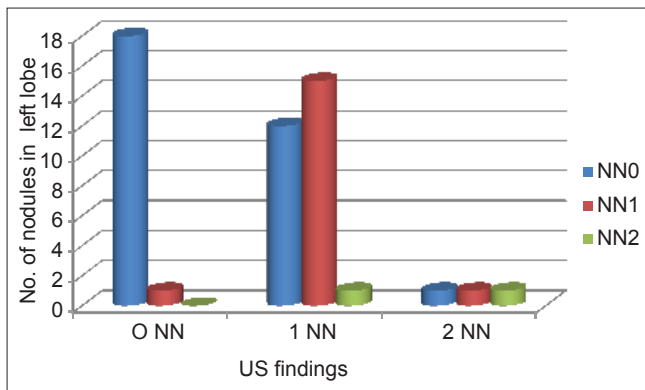
	Surgery
Chi-square	16.840
Difference	2
Asymptomatic significance	0.000

**Graph 8: Comparison between ultrasound diagnosis and operative findings****Graph 9: Comparison between total number of nodules by clinical examination and ultrasonography**

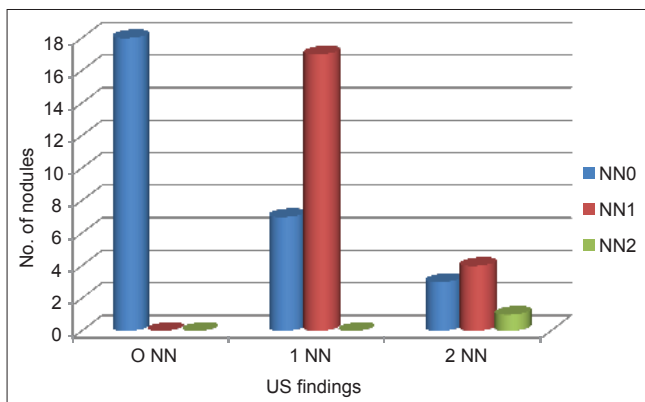
study showing USG leading to a change in management of 44% of patients who had been referred for a solitary nodule on physical examination.<sup>9</sup>

An ultrasound examination focuses on the size of the nodule, its composition, the presence of additional nodules, and any sonographic appearance suggestive of malignancy. Patients with multiple thyroid nodules have the same risk of malignancy as those with solitary thyroid nodules<sup>10</sup> or even diffuse goiters<sup>11</sup> and it is recommended

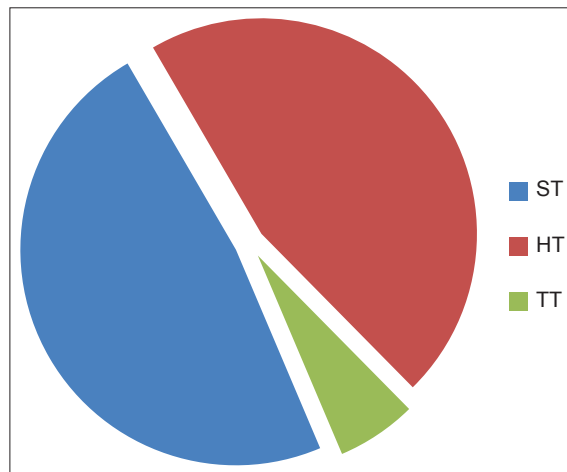




**Graph 10: Comparison between total number of nodules in left lobe by clinical examination and ultrasonography**



**Graph 11: Comparison between total number of nodules in right lobe by clinical examination and ultrasonography**



**Graph 12: The frequency of different surgeries**

that all patients who have a nodular thyroid undergo ultrasound evaluation.

In classification of thyroid disease as diffuse, solitary, or MNG, clinical examination and USG correlated significantly. However, only one third of the clinically

solitary nodules proved to be solitary by ultrasound examination. Of 77 separate nodules, 43 escaped detection on clinical examination. Of these 43, 14 nodules exceeded 2 cm in diameter. It is concluded that the use of USG frequently alters the primary evaluation of thyroid nodularity based on palpation.<sup>12</sup>

US proved to be especially valuable for differentiating between solid and cystic nodules. This is of practical importance because completely cystic nodules are nearly always benign and may be treated by thin needle puncture with aspiration of cyst fluid. In addition, USG is of some value in making a better functional classification of nodules, better estimating the size of the thyroid and in the follow-up of patients with various thyroid disorders who are under treatment of untreated.<sup>13</sup>

In patients with short, fat necks, nodules may be extremely difficult to detect.<sup>14</sup>

A prominent but normal thyroid gland in a patient with thin neck may be perceived by the examiner as an abnormality of the thyroid,<sup>15</sup> the sensitivity of palpation of the thyroid gland in terms of size and nodularity was 38%.<sup>16</sup>

Current USG technology permits high-resolution imaging of the thyroid gland that is more accurate than clinical palpation or other imaging techniques.<sup>17,18</sup> USG is safe and sensitive and is capable of detecting lesions as small as 1-3 mm in thyroid parenchyma.<sup>19</sup> Katz and colleagues reviewed the accuracy of thyroid USG in 28 thyroid glands examined at autopsy. The correlation between the USG finding of thyroid nodules and the pathologic finding of adenomatous goiter was good; USG thus had a sensitivity of 89% and a specificity of 84%.<sup>20</sup>

Recently, two retrospective studies with 799 and 1475 nodules, respectively, have suggested that micro classifications is the only USG finding predicting histological malignancy.<sup>21,22</sup> Blurred margins, hypoechoic pattern and intra-nodular vascular flow have also been associated with malignant lesions in some (but not all) investigations.<sup>10, 24-27</sup>

Mandel *et al.* studied correlation between ultrasound findings with physical examination in patients with solitary thyroid nodule detected by palpation. 16% of such patients had no corresponding nodule evident on USG and 45% of such patients had an additional nodule detected by USG.<sup>28</sup>

The USG diagnosis correlated with the operative finding in 100% of cases indicating USG examination to be the gold standard one. For 24 (48%) patients sub-total thyroidectomy

was done and in 23 (46%) patients hemithyroidectomy was done. Total thyroidectomy was done in 3 (6%) patients.

Most of the nodules were present in the upper pole of the thyroid lobes, next common was in the middle pole and least was in lower pole. The clinical diagnosis was different when nodule was present in pole for 9 times, middle pole for 10 times and lower pole for 7 times. In a study conducted by Gerry *et al.*, it was revealed that nodule located deep or in the posterior aspect is difficult to palpate clinically the nodules over isthmus is easy to palpate than a nodule in the upper pole. 12 nodules of size 1 cm or less, 4 nodules of size 1.5 cm, 4 nodule of size 2 cm and 3 nodules of size 3 cm were diagnosed by USG which was not detected by clinical examination.

The probability of by malignancy by ultrasound was present in cases out of which 3 cases eventually was diagnosed as carcinoma by histopathological examinations. The most common variety of goiter was colloid, which was followed by adenoma and hashimoto thyroiditis.

The study showed that in 52% of cases the clinical diagnosis was confirmed by ultrasound and in the rest 48% of cases the diagnosis and management was changed because of the use of USG.

## CONCLUSION

Majority of the patients were females and belonging to the age group between 20 to 50 years (88%). Out of 50 cases, clinical diagnosis correlated with USG diagnosis in 26 cases which accounts for 52% of cases and in the rest 48% of cases the diagnosis and henceforth the management changed.

The USG diagnosis correlated exactly with the operative findings indicating it to be the gold standard investigations. When the size of nodule was less than 2 cm, clinical palpation failed to detect it 20 times and 3 times in 3 cm nodules, indicating nodules less than 3 cm are frequently missed by clinical palpations.

The type of nodules was mostly cystic, clinical palpations was correct in almost all cases. Nodules were present commonly in the upper pole followed by middle and lower pole. There was no much significant difference between the sight of the nodule and difficult in detecting the nodule by clinical palpations.

USG gave a suspicious for malignancy in 7 cases in out of which 3 cases (43%) were confirmed to be carcinomatous by histopathological examinations.

Overall research study showed that using ultrasound will change the diagnosis and management in 50% of cases, but the efficacy in detecting malignancy is still debatable.

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# Management of Temporomandibular Disorders using Prolotherapy: A Review of Current Concepts

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## Abstract

Temporomandibular disorders (TMDs) are commonly encountered in general dental practice. These are painful and adversely affect the quality of life. Prolotherapy (PrT) is a minimally invasive procedure that has been found to be beneficial in patients suffering from TMD. The aim of this article is to discuss PrT in detail with a detailed review of the literature. Search was conducted using the internet-based search engines and scholarly bibliographic databases with key words such as PrT, TMD, pain, quality of life, and minimally invasive. Information pertaining to PrT in the management of TMD along with the patho-physiology of TMD pain, history, principle, technique, indications, and contraindications of PrT was described in detail. PrT has been in use in the management of TMD since 1930s. It has been found effective by many practitioners and had the advantage of stimulating fibrous tissue growth along with being minimally invasive. However, more evidence is required in conferring this management modality as a favored one.

**Keywords:** Pain, Prolotherapy, Quality of life, Temporomandibular disorders

## INTRODUCTION

Temporomandibular disorder (TMD) is a collective term describing various clinical problems involving the muscles of mastication, the temporomandibular joint (TMJ), and the associated structures.<sup>1</sup> The TMJ or the craniomandibular articulation with mandibular condyles and squamous temporal bones as the bony elements is a complex joint both morphologically as well as functionally. Disorders of TMJ are painful and are also responsible for the decrease in quality of life.

With the exception of traumatic etiology, the exact cause of most TMDs remains either largely unknown or speculative.<sup>2</sup> Various management modalities have been used to relieve the patients of the pain and discomfort secondary to TMDs. Among these, Proliferative injection therapy (also called as prolotherapy (PrT), regenerative injection therapy) has been in use over the last 65 years.<sup>3</sup> It involves the injection of a medicament at the tendon and ligament insertions in order to stimulate fibrous tissue proliferation.<sup>4</sup> The purpose of PrT in TMD management is to enhance tendon, ligament, and joint healing.

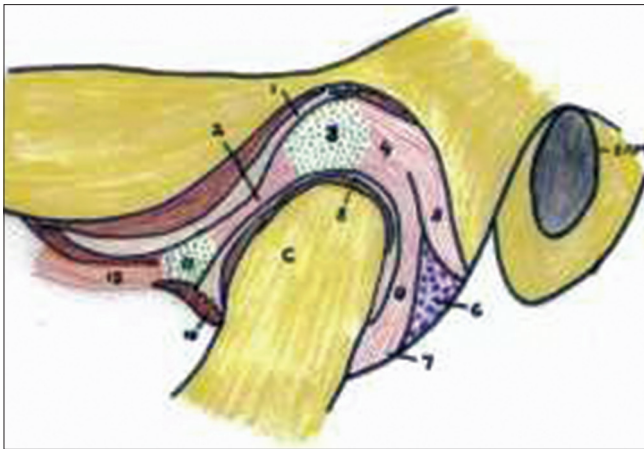
## TMJ Anatomy

The TMJ represents an articulation of the mandible to the temporal bone with a dense fibrous connective tissue called as the “articular disc” separating the bony components (Figure 1). Anteriorly, the articular disc continues as the anterior attachment and is fused to the capsule of TMJ. Posteriorly the disc continues as the posterior attachment or bilaminar zone. The articular capsule attaches laterally to the articular tubercle. This reinforced lateral portion of the capsule is called the temporomandibular ligament. The sphenomandibular ligament (SML) and the stylomandibular ligament (STML) are the two accessory ligaments of the two accessory ligaments of the TMJ complex (Figure 2). The SML arises from the spine of the sphenoid bone and is inserted on the mandible at the mandibular lingual. The STML is a reinforced sheet of the cervical fascia that extends from the styloid process and stylohyoid ligament to the region of the mandibular angle.

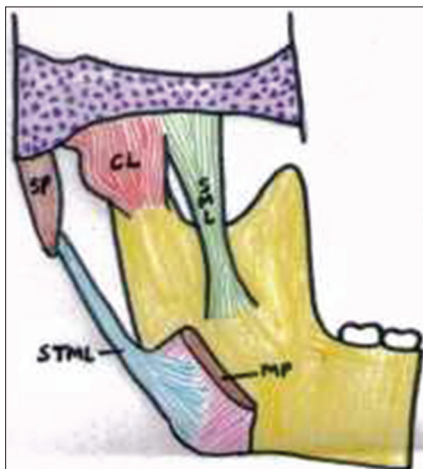
## Patho-Physiology of TMJ Pain

Pain, as defined by the task force on taxonomy of the international association for the study of pain is “an unpleasant sensory and emotional experience associated





**Figure 1: Parasagittal section of temporomandibular joint:**  
C-mandibular condyle, EAM - External auditory meatus,  
1 - Superior joint compartment, 2 - Intermediate zone,  
3 - Posterior zone, 4 - Bilaminar zone, 5 - Upper portion of  
bilaminar zone, 6 - Spongy tissue, 7 - Posterior portion of joint  
capsule, 8 - Inferior joint compartment, 9 - Lower portion of  
bilaminar zone, 10 - Anterior portion of joint capsule,  
11 - Anterior band, 12 - Portion of superior head of lateral  
pterygoid muscles



**Figure 2: Medial view of the mandible:** SP - Styloid process,  
CL - Capsular ligament, SML - Sphenomandibular ligament,  
STML - Stylomandibular ligament, MP - Medial pterygoid  
muscle

with actual or potential tissue damage or described in terms of such damage.” The most common cause of TMJ pain is myofascial pain dysfunction syndrome and primarily involves the masticatory muscles.<sup>5</sup> A known cause of persistent muscle spasms and myofascial pain dysfunction is the underlying ligament laxity.<sup>6</sup> Substantial elongation of the fibrous tissue occurs when there is a rupture of a portion of the inelastic collagen fibers within the tissue. As a result, there is hypermobility of the joint allowing excessive strain on the sensory nerves, which results in nociception at the fibro-osseous junction that is perceived as joint pain.<sup>7</sup> Over a long span of time, hyperfunction, and parafunction are also capable of causing tendon and

ligament rupture and elongation.<sup>8</sup> Ligament rupture or elongation is defined as permanent injury as collagen fibers generally heal incompletely while the elastin fibers do not heal at all.<sup>9</sup> Since it is difficult to immobilize the TMJ without surgical inter-maxillary fixation, continued function on injured joint aggravates and complicates the injury.

## HISTORY OF PrT

Hackett and Hemwall are considered as pioneers of PrT.<sup>10</sup> Hackett began performing PrT as early as 1939.<sup>7</sup> In fact, he was the first to scientifically demonstrate the strengthening of ligaments by the injection of a proliferative solution.<sup>11</sup> Gedney have also published many articles on their experiences performing PrT.<sup>3</sup> Incidentally, the first published article on PrT focused on treating the TMJ.<sup>12</sup>

## PRINCIPLE OF PrT

Webster’s third new international dictionary describes PrT as “the rehabilitation of an incompetent structure, such as a ligament or tendon, by the induced proliferation of cells.” PrT is based on the concept that the cause of most chronic musculoskeletal pain is ligament and/or tendon laxity. PrT uses an inflammatory mimetic that re-initiates the inflammatory process in the joint thus, stimulating fibroblast proliferation thereby augmenting the healing process and strengthening the joint, tendons, and ligaments.<sup>4</sup>

## MECHANISM OF ACTION OF PrT

The process of inflammation plays a crucial role in wound healing. In the event of an injury, inflammatory cells such as the granulocytes, monocytes, and macrophages migrate to the injury site. Fibroblasts are activated by the growth factor that is released, and they produce matrix and new collagen fibrils.<sup>13</sup> But these collagen fibrils do not align with the original connective tissue. Instead, they grow at right angles to the plane of the injury. The integrity of the zone of healing is further compromised as the elastin fibers do not heal at all. Anti-inflammatory medications usually prescribed after injury allay pain and swelling but unfortunately they diminish the healing response.<sup>4</sup> As a result of this incomplete healing, the joint remains painful with normal or even sub normal physical activity. Such a joint may become hypermobile and prone to re-injury due to incomplete ligament support.

In PrT, an inflammatory mimetic agent like dextrose is injected into the joint to initiate low-grade inflammation.

Fibroblast proliferation is initiated, and the osteoprogenitor cells present in the periosteum lay down reparative bone at the fibro-osseous junction, further strengthening the connective tissue attachment. Repair at the fibro-osseous junction is also facilitated by the periosteal blood flow which is critical considering the relative avascularity of the tendons and ligaments.<sup>14</sup> Dextrose is also thought to increase the production of growth factor by generating an osmotic gradient.<sup>4</sup>

PrT may also be beneficial in TMD management owing to its anti-microbial effect. Chlamydia, *Mycoplasma genitalium*, *Staphylococcus aureus*, *Mycoplasma fermentans*, *Actinobacillus actinomycetemcomitans*, and *Streptococcus mitis* have been cultured from the TMJ. The presence of *S. aureus* in the TMJ synovial fluid has been related to TMD.<sup>15</sup> The bacteriostatic water used in PrT along with the osmotic concentration produced may inhibit the growth of and/or kill these organisms.

## CONSTITUENTS OF PrT SOLUTION<sup>10</sup>

The PrT solution consists of four agents—an osmotic agent, an inflammatory mimetic, a chemical irritant, and a physical irritant. Dextrose is most commonly used in a concentration of 12.5% as an osmotic agent, prepared by diluting one part of 50% dextrose in 1% methyl paraben (preservative) with two parts of 1% free lidocaine and one part of bacteriostatic water. Sodium morrhuate serves as the inflammatory mimetic attracting the inflammatory cells at the site of injection. Phenol and pumice flour serve as the physical and chemical irritants, respectively, attracting the macrophages and granulocytes by either foreign body reaction or cell wall damage/alteration.

## TECHNIQUE OF PrT FOR TMD<sup>4</sup>

A reclined or supine patient position is preferred to provide head stability. The head is turned to the opposite side away from the injection site. An antiseptic is used to cleanse the skin before marking the anatomical marks. Patient is asked to close the anterior teeth by biting on two small bite block thus, providing access to the superior joint space. A 3cc syringe with 30-gauge needle and 1-inch length is chosen to penetrate the skin midway between the tragus and the posterior aspect of the condyle, directing it superiorly and anteriorly toward the superior joint space where it makes contact with the periosteum where a little resistance is felt. A common schedule is at an interval of 2, 4, and 6 weeks over a total of 12 weeks. The injection site is checked for bleeding after withdrawal of the needle, and the patient is allowed to rest for some time.

## INDICATIONS OF PrT<sup>16,17</sup>

- Evidence of a tendinous or ligamentous injury or disorder
- Willingness of the patient to undergo the injection therapy irrespective of the discomfort
- In refractive cases where conservative management like-medical, physical, dietary, home care therapy have failed
- Where surgical management is not possible
- To enhance recovery as an adjuvant to other treatment procedure like oral appliances.

## CONTRAINDICATIONS OF PrT<sup>18</sup>

- Allergy to the components of PrT solution
- An active infection at the site of injection
- A healing disorder
- Conditions associated with excessive bleeding like hemophilia
- A malignant condition
- Presence of parafunctional habits.

## SIDE EFFECTS AND POTENTIAL COMPLICATIONS

In some cases of PrT, a temporary posterior open bite may result due to the distraction of the condyle and mandible inferiorly secondary to the introduction of the injection fluid into the articular space. If there is a rapid reduction of a displaced disc, it may lead to permanent occlusal changes with teeth settling into solid occlusion through passive eruption.<sup>18</sup> Orthodontic or prosthodontic correction may then be needed in these cases to stabilize the occlusion. Postinjection morbidity may result from a faulty injection technique. With TMJ PrT, some potential complications include discomfort during the procedure, temporary anesthesia extending as far as the eye leading to ptosis, external bleeding, or facial bruising.

## CONCLUSION

PrT has been shown to be an efficient and conservative method in the management of TMDs. By stimulating ligament and capsular repair, it represents a more permanent solution to the persistent and refractory problems associated with the TMJ.<sup>19</sup> Since fibrous tissue proliferation may continue for as long as 18 months, patience of both the practitioner as well as the patient is important.

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# Diagnostic Aids of Precancerous Oral Lesions

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## Abstract

Early detection of oral cancer is the key to survival. The most effective method of combating oral cancer is early detection, diagnosis and eradication of early-stage lesions and their precursors. Historically, the screening of patients for signs of oral cancer and precancerous lesions has relied upon the conventional oral examination. A variety of commercial diagnostic aids and adjunctive techniques are now available to potentially assist in the screening of healthy patients for evidence of otherwise occult cancerous change or to assess the biologic potential of clinically abnormal mucosal lesions. Advances in diagnosis and staging at the molecular level are expected to affect choice of treatment and patient outcomes. The realm of oral cancer and pre-cancerous lesions detection adjuncts and tests is an exciting and constantly progressing area of research and technology. Integration of the adjuncts and tests discussed here can help uncover hidden lesions before they have the chance to progress into malignancy, and hopefully improve patients' chances of living a long, healthy life.

**Keywords:** Cytology, Diagnosis, Oral cancer, Pre-cancerous, Squamous cell carcinoma

## INTRODUCTION

Oral squamous cell carcinoma (SCC) is the most common cancer of the head and neck.<sup>1</sup> A key factor in the lack of improvement in prognosis over the years is the fact that a significant proportion of oral SCCs are not diagnosed or treated until they reach an advanced stage. This diagnostic delay may be caused by either patients (who may not report unusual oral features) or health care workers (who may not investigate observed lesions thoroughly).<sup>2-4</sup>

Early evaluation of oral pre-cancerous lesions can have a dramatic impact on oral cancer mortality rates.<sup>5</sup> Detection of oral cancer in the early asymptomatic stage dramatically improves cure rates and patient's quality of life by minimizing extensive, debilitating treatments. The 5 years survival rate for patients with early, localized disease approximates 80%; for those with distant metastases, it is 19%.<sup>6</sup> Unfortunately, more than 50% of patients with oral cancer display evidence of spread to regional lymph nodes and metastases at time of diagnosis, and approximately two-thirds of patients have apparent symptoms, a negative prognostic indicator.<sup>7</sup>

Pre-cancers and early-stage oral cancers cannot be adequately identified by visual inspection alone and easily

may be overlooked and neglected, even by highly trained professionals with broad experience.<sup>8</sup> The most effective method of combating oral cancer is early detection, diagnosis and eradication of early-stage lesions and their precursors.<sup>9</sup>

The diagnosis and treatment of oral premalignant lesions and SCC are currently based on histopathological features, site of involvement and stage of disease. Recent advances in techniques for detecting lesions and predicting their progression are reviewed here. Advances in diagnosis and staging at the molecular level are expected to affect the choice of treatment and patient outcomes.

## EARLY DETECTION OF PRE-CANCEROUS ORAL LESIONS

### Clinical Examination

Clinical examination for oral premalignant lesions and SCC should include a thorough head, neck and intraoral examination, with examination of the cervical lymph nodes and visual examination and palpation of the oral mucosal surfaces. The location, size, border, color, and surface characteristics of any lesion should be recorded, so that future changes can be recognized. When a biopsy is



performed, site selection is critical, as the histologic features may vary in non-uniform lesions.<sup>1</sup>

### Exfoliative Cytology

Oral biopsy represents the gold standard for determining the nature of a mucosal lesion and for diagnosing SCC, and exfoliative cytology has, until recently, been discounted as a tool for assessing oral mucosal lesions. However, techniques have now been reported that include evaluation of exfoliated oral epithelial cells and comparisons of these methods with biopsy techniques. Exfoliative techniques have the advantage of being minimally invasive, and they do not require a local anesthetic. Use of a cytobrush reportedly allows sampling of the full thickness of stratified squamous epithelium of the oral mucosa.<sup>10</sup>

### The Brush Biopsy

Today pap smears are used effectively for oral red lesions and oral ulcers to identify infections, especially candidiasis, and atypical cells in erythroplakia. The brush biopsy or Oral CDx test is relatively painless procedure captures the deeper epithelial cells on the bristles and the entire brush is sent to a pathology laboratory, where the cells are removed and plated on a microscopic slide. From that point on, the process is the same as a routine pap smear. A cytotechnologist, pathologist or, more recently, a computer-associated optical scanner compares the size of each individual cell with the size of its nucleus. Large, dark nuclei are found in dysplastic or immature cells, as are abnormal nuclear shapes (pleomorphism). Results are usually reported out as one of three levels of risk.<sup>11</sup>

### Liquid-based Cytology (LBC)

In recent times, LBC has become a principle methodology in cytopathology replacing conventional smears, owing to better cell recovery and morphologic preservation.

LBC had been adopted to analyze the brush biopsy samples of the oral mucosa. LBC methodology appears to not only increase the sensitivity and specificity of cytologic diagnosis but, significantly, also provides additional samples for immunohistochemical and other molecular studies which are not possible with conventional cytologic smears. The brush biopsy and LBC, as with all adjunctive technologies for oral dysplasia, must be used with intelligence and its routine use requires that the clinician be relatively knowledgeable about the clinical features of pre-cancers and can properly identify the most "severe" area to brush.<sup>11</sup>

### Toluidine Blue *In vivo* Staining of Deoxyribonucleic Acid (DNA)

Toluidine blue (tolonium chloride) is a metachromatic dye long used in histology laboratories to stain nuclear material,

since it stains DNA very well. This test is premised on the fact that mucosal cells with extra DNA, i.e. large nuclei, attract and retain the stain, even after the bulk of the stain has been washed off with acetic acid.<sup>12</sup>

Unfortunately, this dye test is awkward to use, requiring an acetic acid (vinegar) rinse before and after, and there are high proportions of false positives and false negatives.<sup>13,14</sup> It frequently needs to be repeated because the false positive tests are often trauma-or inflammation-related. Moreover, the dysplastic cells lying deeply in a thick keratotic lesion will likely not be stained adequately. Even with its limitations, however, the toluidine blue test can be a good adjunctive test in the hands of an experience, knowledgeable clinician, and is especially effective with erythroplakia and carcinoma *in situ*.<sup>13,14</sup> It should not be considered a standalone test and will not give a diagnosis, but it can help to localize areas to biopsy or to brush biopsy.

### The ViziLite-Highlighting the Keratin

In the oral environment, acetic acid makes the keratin more white and, therefore, more visible to the naked eye. A thin leukoplakia which might otherwise have been missed could be detected after a minute of contact with acetic acid. The ViziLite(R) system takes advantage of this and adds bright blue light to even further enhance keratin detection.<sup>15-17</sup> This technology uses reflected light solely and so can only give us information from the most superficial cell layers. The light is derived from either chemical tubes (chemiluminescence) or a laser and recently, toluidine blue has been added to the kit (ViziLite Plus(R)) for identification of superficial nuclear abnormalities. As with other adjunctive diagnostic technologies, the ViziLite(R) exam has disadvantages. It seems to have a high proportion of false positive and false negative tests, relative to identification of dysplastic cells rather than hyperkeratosis.<sup>17,18</sup> As an adjunctive test, this system is valuable in that it increases awareness of the oral cancer and pre-cancer detection dilemma for both the clinician and the patient.

### Oral Autofluorescence-When the Mucosa Doesn't Glow

Two optical devices, the VELScope(R) and Identify(R) take advantage of the fact that, to a certain degree, we all glow. Each of our cells contains molecules capable of self-fluorescence, especially when activated (excited) by specific light waves.<sup>19-23</sup> Excitation and emission of fluorescence depends on how light is scattered and absorbed in tissue: Scattering is caused by differences in the index of refraction of different tissue components, while absorption is dependent on the molecular composition of the same components.<sup>21-23</sup> In humans, these fluorescing products are numerous: Tryptophan, porphyrins, collagen cross-links, elastin, nicotinamide adenine dinucleotide (NADH), and flavins, flavin adenine dinucleotide (FAD)<sup>23</sup> This fluorescent

signaling has been used to assess the metabolic state of tissues and to identify primitive/dysplastic cells.

The amount of fluorescence given off from living tissues is very slight; certainly not capable of being seen under normal conditions. However, if violet or blue light is used in a darkened room and the clinician peers through the eyepiece or pair of glasses which filter out virtually all reflected light and only allows transmission of light of the wavelength(s) of the fluorescing tissues, the autofluorescence is easily seen. The wavelengths which excite the greatest fluorescence in oral mucosa range from 400 to 460 nm, i.e. violet and blue light.

The Identify(R) 3000 Ultra shines a violet light of approximately 405 nm, which especially stimulates a blue/violet fluorescence. The light shines from a battery-powered device roughly the size, shape and weight of a dental handpiece; the user looks through special filtering glasses. This device also provides two other types of light: A white light suitable for a conventional visual examination, and a green-amber light that highlights keratinized mucosa and submucosal blood vessels.

The VELScope(R) uses a blue light with peak intensity at approximately 436 nm; this wavelength especially stimulates a green fluorescence. The device shines light out of a handheld "gun" that is tethered to a light source which typically remains on a cart or countertop plugged to the wall, and the user looks through a filtered eyepiece that disallows reflective and ambient light.

An immature or dysplastic epithelial cell has much less NADH and FAD activity than a normal cell and so mucosal areas with such cells will not fluoresce, thereby appearing black (blackish-green or blackish-blue) through the eyepiece or glasses. In addition, data were also suggests that the cross-links in sub epithelial collagen fibers beneath dysplastic cells also lose fluorescent activity, contributing to the "black spot" seen through the filter.<sup>23</sup>

The beauty of the self-fluorescence test is that the light used to excite the oral cells penetrates to the deepest part of the epithelium and so easily reaches dysplastic cells in the lower regions of the epithelium, as well as the subepithelial collagen fibers. This deep penetration can, however, prove to be a bit of a disadvantage in certain settings, since several nondysplastic tissue changes are also positive with this test.

## CONCLUSION

Since the oral cavity is the only region of the aero digestive tract that can be effectively screened, dentists

should continue to be encouraged to perform oral cancer examinations of all patients. Public education that stresses the importance of yearly oral cancer examinations, identification of the warning signs of oral cancer, and recognition of the hazards associated with tobacco and alcohol use is necessary to reverse the high morbidity and mortality rates associated with this disease.

Molecular techniques are expected to aid in diagnosis and staging of the disease, and in providing intermediate markers to assess treatment interventions. In addition, advances in knowledge may lead to new therapies, ultimately improving the management of at-risk lesions once they are identified, as well as improving the prevention and management of SCC. Combining information from molecular markers with exfoliative techniques may overcome some of the current limitations of exfoliative cytology. These combined techniques may prove to be sensitive and specific procedures that can be performed sequentially over time and perhaps as screening methods for at-risk lesions already identified.

Molecular markers are expected to become essential in the diagnosis and management of patients with oral cancer; they will guide future study and clinical care and will ultimately lead to new interventions directed at the molecular changes of cancer. Use of these technologies allows earlier diagnosis and staging of tissue change, before changes in cell morphology occur and certainly before tissue changes become clinically visible. Ultimately, the use of various diagnostic aids may lead to better survival and less treatment-associated morbidity through early recognition of and intervention for at-risk oral lesions.

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# Hypericin Over Aminolevulinic Acid - A Photosensitizer for Diagnosis of Potential Malignant Disorders and Early Oral Cancer: A Review

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## Abstract

It is important to develop a rapid and accurate means for the detection of early oral cancer. More recently, a new technique is introduced which uses hypericin (HY), a plant based photosensitizer that accumulates selectively in abnormal cells, including tumor cells and emits red fluorescence indicative of selective uptake when compared to normal tissue that enables to diagnose oral cancers. This review tends to highlight the sensitivity and specificity of HY over aminolevulinic acid and the application of HY in diagnosis of oral potential malignant disorders and early oral cancer as compared to standard techniques in day today practice.

**Keywords:** Diagnosis of oral cancer, Hypericin, Photosensitizer

## INTRODUCTION

The most common cancer of the oral cavity is squamous cell carcinomas (SCC) and South Asia has relatively very high incidence rates. The main high-risk groups are adult men and women<sup>1</sup> who use tobacco, alcohol, and betel nut, which lead to many other potentially malignant disorders (PMD). SCC is usually preceded by dysplasia presenting as white, red or mixed red, and white epithelial lesions on the oral mucosa (leukoplakia, erythroplakia). Malignant transformations occur in 1-40% of patients with leukoplakia and 1-90% patients of erythroplakia over 5 year.<sup>2</sup> Thus, routine oral and dental examinations can help in the detection of oral PMD at an early stage.

The early diagnosis of PMD can reduce mortality,<sup>3,4</sup> thereby it becomes important to develop a rapid and accurate means for the detection of early oral cancer.<sup>1</sup>

The paper aims to review and highlight the non-invasive diagnosis of oral potential malignant disorders and early

oral cancers using hypericin (HY), a photosensitizer that would enable monitoring and detection of these oral lesions at routine dental and oral examination.<sup>5</sup>

Conventional methods of diagnosis of oral PMD and malignancy are mainly done by visual examination and biopsy. It is the standard method of revealing PMD and SCC. The current approach to detecting the transformation of PMD to carcinoma is regular surveillance combined with biopsy or surgical excision. However, visual examination provides very poor diagnostic accuracy while biopsy techniques are invasive and unsuitable for regular screening and also time consuming slow process, requiring several days.<sup>1,6</sup>

Several studies have investigated the use of vital staining with agents such as lugol iodine, toluidine blue, and tolonium chloride for detection of oral malignancy. Sensitivity of these agents is in the hands of experts that provides approximates 90% and rapidly decreases when used by non-experts such as screeners. The specificity of these agents is poor.<sup>7-9</sup>



## Photosensitizers

A photosensitizer is defined as a light triggered fluorescent compounds, which upon absorption of light induces a chemical or physical alteration of another chemical entity. The photosensitizer may be synthesized or induced endogenously by an intermediate in heme synthesis, 5-aminolevulinic acid (5-ALA). The photosensitizer commonly used in clinical practice has porphyrin ring structure. These photosensitizers generally have higher affinity and accumulate in the fast proliferating cancer cells than normal cells.<sup>10</sup>

Studies showed that these photosensitizers were used in the photodynamic therapy (PDT) to eradicate cancerous cells due to its high affinity and preferential uptake by tumor cells. The same property of photosensitizers could be used as a promising biomarker in the diagnosis of PMD and early oral cancer. Such diagnoses are commonly referred to as photodynamic diagnosis (PDD). PDD of PMD and early cancer has found its way into clinical use and has been extensively studied.<sup>11-14</sup>

Main properties of photosensitizer used in PDD:

- Homogeneity.
- High affinity to lesions.
- High-fluorescence quantum yield.<sup>15</sup>
- Rapid pharmacokinetic elimination.
- Low levels of dark-toxicity.<sup>16</sup>

HY, which is excited at 590 nm is a plant-based photosensitizer,<sup>5</sup> and has evolved in fluorescence diagnostic imaging of oral lesions. *Hypericum perforatum* (St. Johns Wort) is a plant found in the regions of moderate climate of Europe, South America and in India.<sup>17</sup>

## Constituents of HY<sup>18</sup>

- HY
- Pseudohypericin
- Flavonoids
- Biflavones
- Hyperforin
- Tannins
- Procyanidines
- Xanthones
- Other constituents: Chloregenic acid, caffeoylquinic, and p-coumaroylquinic acids.

Topical or systemic application of photosensitizers can render pathologic tissues fluorescent when exposed to specific wavelengths of light.<sup>19</sup> Fluorescence diagnosis of oral cancer utilizes the characteristic fluorescence signatures, either from endogenous or exogenous fluorophores, to distinguish abnormal tissues from surrounding normal tissues. If the fluorescence signatures use endogenous

biomolecules then, the diagnostic technique is termed as auto fluorescence diagnosis and if exogenous fluorescence are used in the diagnosis, then its exogenous fluorophores.<sup>20</sup>

## Endogenous Fluorescence

Most of these endogenous fluorophores are weak fluorescence when excited optimally by ultraviolet (UV) blue region (300-450 nm). In addition, high-tissue scattering and strong absorption of hemoglobin in 400-500 nm region often limit the penetration depth of UV-blue light in tissue.<sup>21</sup> The epithelial thickening, which typically occurs in tumors, can further reduce the amount of excitation light reaching the inner sub-mucosa where most endogenous fluorophores are located.<sup>13,22</sup> Collagen and reduced nicotinamide adenine dinucleotide are the best examples.

## Exogenous Fluorescence Diagnosis

These are synthetic fluorophores, which are excitable at longer wavelength and are used to visualize neoplastic lesions that cannot be seen with white-light imaging and auto-fluorescence.<sup>23</sup> HY and ALA are evaluated for its clinical application.

## HY and its Photodynamic Properties

HY consistently exhibits fluorescence maxima at around 590 and 640 nm. With absorption maxima of HY being at longer wavelength, allow excitation light to reach HY in deeper tumors.<sup>13</sup>

HY-induced PDD has been first used in detecting flat carcinoma *in situ* lesions of the bladder.<sup>24</sup> Thereafter, the applications of HY were also extended to diagnose oral cancer and stomach cancer.<sup>1,25</sup>

The most important defining property of HY as photosensitizer in PDD is its photo stability and its fluorescence that could be detected for up to 16 h after administration as compared to 5-ALA that has fast photo-bleaching action, less tissue penetration due to low lipophilicity and lower specificity.<sup>26</sup>

HY exhibits tumor selectivity because of its mechanical properties such as diffusion and endocytosis.<sup>27</sup> Study has showed that HY has nearly 3 times higher intensity for Grade 3 cancerous cells than of Grade 1 cells.<sup>28</sup>

## Sensitivity and Specificity between HY and 5-ALA

The diagnosis with 5-ALA has sensitivity between 78% and 100% when compared to HY, which is between 82% and 94%.<sup>29</sup> ALA was shown to yield low specificity ranging from 41% to 66% and so many give false positive results when compared with HY.<sup>23</sup> On the other hand, HY has superior specificity ranging from 91% to 98% and this greatly reduces the incidence of false positive results.<sup>24,29</sup>

### Advantages of Fluorescence HY over Standard White Light Endoscopy (WLE) (Figure 1)

- Facilitating guided biopsies and reducing the number of biopsies.
- Providing visualization of tumor margins during surgical procedures.
- PDD allows noticing very small foci of early cancer lesion and PMD, which are visible as the red fluorescence dots on the green oral mucosa background.
- Same-day diagnosis and cancer staging in a clinical setting.<sup>1</sup>

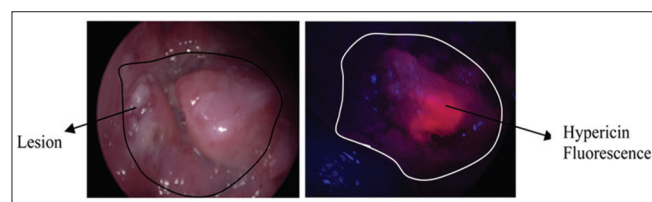
### Fluorescence Endoscopy (FE)

FE is the use fluorescence photosensitizer in endoscopy as it can easily overcome the shortcomings of WLE.<sup>30</sup> The mean value of the sensitivity for FE is 93% compared to only 73% for WLE.<sup>23</sup> The FE system uses excitation filter chosen to exactly match its absorption peak, and the resulting fluorescence emission could be specifically filtered for sole detection of photosensitizer fluorescence. This filtered fluorescence photosensitizer is finally interfaced to a PC for image acquisition and final analysis. The acquired fluorescence images are first pre-processed to extract the region-of-interest (ROI). The ROIs, are then extracted and expressed in terms of the color intensity as with red (IR), green (IG), and blue (IB) as well as the hue and saturation (HS) values.<sup>1,31</sup>

### Clinical Study of Oral Disease with PDD

Photosensitizer application to PMD was studied by K Jurczyk *et al.* where in the series of photographs were taken with white light, UV light, and Blue light using Hoya filters. The images with blue and UV light using the orange filter were taken and in both cases total areas of the lesion appeared to be larger than it has been clinically observed.<sup>15</sup>

In a study conducted by PSP Thong *et al.*, 23 patients were examined by FE using HY solution (100 ml) that was topically administered to each patient by oral rinsing over 30 min. The entire oral mucosa was HY photosensitized, however, the oral mucosa with lesions showed to retain HY for a longer period of time compared to the normal oral mucosa. At 2 h after topical application, most normal tissues tend to have cleared HY, whereas abnormal lesions still show fluorescence.<sup>1</sup>



**Figure 1: White light (left) and hypericin image (right) of the oral lesion acquired using a fluorescence endoscopy system**

The IR/IB and IR/IG ratios were calculated for each image. These mean image parameters were used to distinguish the tissue type at three levels:

- Normal versus hyperplastic tissue
- Normal versus SCC tissue; and
- Hyperplastic versus SCC lesions.

### Discussion of Image Colors (Figure 2)

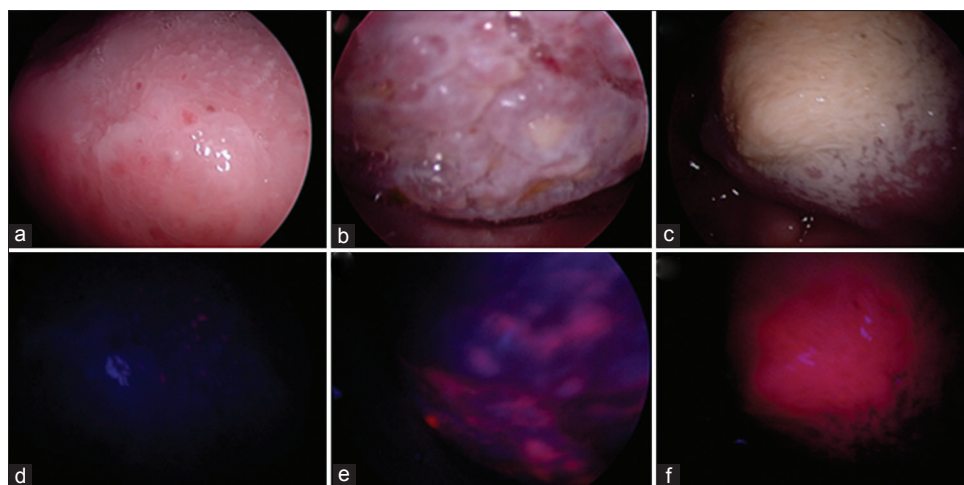
- Red fluorescence was observed in lesions, indicating a selective uptake of HY in lesions compared with normal tissue. SCC tissue is most likely to be ulcerated and inflamed resulting in brighter fluorescence compared with normal tissue.
- The IR/IB ratio is a good image parameter for distinguishing between normal and hyperplastic tissues with the sensitivity and specificity of 100 and 96%, respectively; normal from SCC tissues with sensitivity and specificity of 100%, respectively; and hyperplastic from SCC with 92 and 90%, respectively.<sup>1</sup>
- The IG/IB ratio is not a good image parameter for distinguishing tissue types.
- The IR/IG ratio, which is the ratio of tissue fluorescence to auto fluorescence, could distinguish between normal and hyperplastic tissue and normal to SCC tissue.<sup>1</sup>

False positive results are observed in hyperplasia of the tongue (histologically confirmed presence of Candida) that is known to take up fluorescent dyes.<sup>32</sup> al-Bagieh, 1991 another condition like benign neoplasia of salivary gland, pleomorphic adenoma of the palate there may be an accumulation of higher level of photosensitizer, than usual.<sup>1</sup>

The use of HY as with PDD and PDT, is now applied in association with nanotechnology for therapeutic purpose and also in multimodality imaging.<sup>20</sup> The technology uses measured optical signals that could be essentially correlated with the pathological status of the tissues that are considered superior to WLE for the diagnosis of various types of cancer, including those in the oral cavity.<sup>28,33,34</sup>

## CONCLUSION

HY is the strongest photosensitizer; it can be used along with WLE that helps in identification of early and flat lesions. HY when used in histopathological observation of tissues, it reduces the time required for examination. The other added advantages include reducing the number of biopsies required by guiding the biopsy procedure and aid in the delineation of tumor margins during clinical procedures. All these properties of HY in PDD could someday make it a promising applicator in the chair side



**Figure 2: Images of tongue. White light images from (a-c) and hypericin fluorescence images (d-f), endoscopic images of normal tongue mucosa (a and d), images of hyperplastic tongue (b and e), images of squamous cell carcinoma of the tongue (c and f). Red fluorescence indicates pathology tissue. Blue fluorescence indicates normal mucosa. The fluorescence images show a progressive increase in the red-to-blue intensity (IR/IB) ratios from normal (a and d) (R/B ratio=0.3) to hyperplastic (b and e) (R/B ratio=1.0) to SCC (c and f) (R/B ratio=2.0) tissue**

detection, conformation, and monitoring of the oral potential malignant disorders and early oral cancers as a rapid and accurate means with no much time consumption.

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# Behavior Management of Dementia Patients: A Review

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## Abstract

It is increasingly achieving concern that pharmacological treatments for dementia should be used as a second-line approach in the comparison of non-pharmacological approach. This review focuses on both pharmacological and non-pharmacological approaches. It highlights the new discovered drugs as well as some traditional non-pharmacological treatments such as behavioral therapy validation therapy and reality orientation etc., and also observes the contribution of other interesting alternatives such as aromatherapy, cognitive therapy, and music therapies, etc. Both of the pharmacological and non-pharmacological treatments have reported welfare in various research studies. Some more reliable and valid data should be collected before the potentials of these approaches are recognized more widely.

**Keywords:** Dementia, Mental health, Psychosocial, Treatment

## INTRODUCTION

Dementia is defined as a generic term indicating a loss of intellectual functions including memory, significant deterioration in the ability to carry out day-to-day activities, and often, changes in social behavior.<sup>1</sup> Dementia is increasingly spreading widely all over the world in many forms with aged persons. In this regard psychologists' interest has grown in the use of psychosocial interventions with traditional pharmacological and non-pharmacological treatment for demented people. An intense review of empirical studies and systematic researches has been accomplished on wide range of such interventions to examine their potentials. Although, a little account has been taken in the regard of the appropriateness of psychosocial interventions for those people, who are in different stages of the illness.<sup>2</sup> Assessment of patient's present condition is helpful, before judging the management and formulating the target behavior. Some major points in the assessment include:

- Cognitive functions-it includes the areas of preserved functions or those areas which have a lesser degree of impairment; it is helpful to identify the person's style of coping and its management.
- Life story-it includes the preferences or choices of the patient.

- Person's behavior is causing distress-what and when circumstances.
- Social network-available resources of social network come in this category.

## TYPES OF DEMENTIA

### Alzheimer's Disease (AD)

AD is the most common cause of dementia. Many symptoms like memory problems, continuous deterioration in the ability to perform daily living basic activities, and changing behavior, social withdrawal and apathy are most common, and behavioral disturbances also. Abnormal function and ultimately death of selected nerve cells in the brain causes AD. The patients have following diagnosis; have an average survival period for 8-10 years.<sup>3</sup>

### Vascular Dementia

The vascular disease has a complex and controversial role in the etiology of dementia is. There seems to be a direct chronological relationship between significantly cerebrovascular events and the onrush of dementia in some cases. Eventually, patients may present with signs of stroke or other vascular problems, i.e., hypertension ischemic heart disease. Onset of dementia may be precipitous, or there may



be sudden declining periods, followed by relative stability. Some physical problems such as decreased mobility, urinary incontinence and balance problems are more common in vascular demented people than those with AD.

### Dementia with Lewy Bodies (DLB)

Most common symptoms of DLB are wavering awareness of day-to-day activities and symptoms of parkinsonism like rigidity, tremor and deceleration of movement or scarcity of expression. Frequent occurrence of delusions or visual hallucinations. Steep descents are also common. DLB is similar in pathological basis to Parkinson's disease dementia, and both of them are associated with successive cognitive deterioration and parkinsonism. It has been reported that after 10 years, about 3/4<sup>th</sup> of aged people with Parkinson's disease acquire dementia.<sup>4</sup>

### Fronto-temporal Dementia (FTD)

It is a type of dementia (FTD) that is exceptional in the comparison to AD or vascular dementia, but symbolizes a significant ratio of people who develop dementia till the age of 65. Changing of behavior like lack of judgment, disinhibition, decline of social awareness and insight are more common in the comparison of memory problems. Mood swings, continence and disturbed speech are frequent. It is rare to have a positive family history of a similar disorder.

### Mixed Dementias

A person can develop a mixture of two or more of the active dementias, which is usually dominating from one to another. Various studies recommend that there is an extremely complex interaction between vascular disease and the central features of AD and that inflexible boundaries between subtypes of dementia may be redundantly unreal. Responding towards treatment or side effects from treatment in patients with mixed dementia may vary from people with a specific diagnosis.<sup>5,6</sup>

### Creutzfeldt-Jakob Disease (CJD)

There is one more uncommon type of dementia known as CJD, which includes the accumulation of an abnormal protein, in which the brain leads to a quick decline of nerve cells. Some common problems such as behavioral and mood disturbance are present in the form of tremor, balance problems and impaired mobility. It has been often found that after the onrush of clinical symptoms of illness, death takes place within 1-2 years.<sup>3</sup>

## SIGN AND SYMPTOMS

Some characteristic features of dementia can be described by deterioration in various cognitive domains and its functions, such as:

- Memory loss (amnesia).
- Disturbed receptive or expressive skills of language and speech (aphasia).
- Imperfection in motor functions (apraxia).
- Unable to identify objects (agnosia) or a familiar face (prosopagnosia).
- Unevenness in executing functions like organizing, planning, sequencing of tasks and abstract thinking.
- Deterioration in daily living activities and social activities.
- Disturbed cognitive functions such as short-term memory loss, which is more severe than episodic memory loss.
- Impaired attention and concentration, disorientation of judgment and impaired semantic memory.
- Increased delusions and hallucination with paranoid ideas associated with various things and persons.
- Inappropriate and distracted behavior, restlessness, sexual disinhibition and lack of interests.
- Irritability, anxiety, depression and liability.
- Dysomnia or parasomnia.<sup>7,8</sup>

## STAGES OF DEMENTIA

Three main stages of dementia have been studied till now in a broader perspective. It is very difficult to be ensured the onset of the illness and the exact timing of the transformation of one stage of dementia to the next one.

- The patient may be considerably more apathetic, lose his interest in leisure and hobbies, find the simple tasks more complex and difficult, and have impaired memory in the early stage of dementia. Delusions and hallucinations take place, which results in blaming on others for stealing and misplacing the things. Depression is one of the major sign, which is due to the loss of insight and disturbed cognitive functions.
- In the mild dementia, cognitive symptoms are more frequent, and self-care is progressively become problematic. Behavioral and psychological disorder such as aggression, agitation, and psychosis are more obvious to occur at this stage of dementia.
- The patient requires 24 h care for routine functions such as bathing, changing of clothes and toileting in a severe stage of dementia. Difficulties in physical problems like walking and talking, and involuntary urination and defecation may also be seen. Sleep disorders, agitation and aggressive behavior are frequent in this stage of illness. The patient becomes bedfast in the last few weeks of his life.<sup>9</sup>

## CAUSES OF DEMENTIA

- Idiopathic or degenerative-DLB, AD and Huntington's chorea, etc.

- Head injury.
- Intracranial lesions-such as subdural hematoma, brain tumor.
- Vascular.
- Infections-such as neurosyphilis.
- Hormonal or metabolic dysfunction-such as hypothyroidism and severe kidney disease, etc.
- Intoxication through drug or alcohol.
- Lack of appetite or anoxia - e.g. after cardiac arrest or carbon monoxide poisoning.
- Vitamin deficiency - e.g. B12.<sup>8</sup>

## TREATMENT

There are mainly two forms of treatment of dementia, which are as follows: Pharmacological and non-pharmacological. Management of behavioral disturbance should be done through both pharmacological and non-pharmacological approaches. The pharmacological interventions are usually considered as much competent etiology of the behavioral disturbance than non-pharmacological, but it may be problematic if delirium is treated through antibiotics as an underlying infection. Depression (one of the major sign of dementia) is reduced by using antidepressants, but before applying the pharmacological approach, non-pharmacological approaches should be considered as a first step in the intervention of dementia.<sup>10</sup>

## NON-PHARMACOLOGICAL TREATMENT

Non-pharmacological interventions are used to ensure the underlying causes of behavioural disturbance of dementia. It is also used to explore and to provide personalised approaches to treat behavioral and psychological symptoms or neuropsychiatric symptoms of the illness. In this section, the therapeutic interventions which are usually assessed in clinical trials are listed here in alphabetical order.<sup>1</sup>

### Behavior Management

Behavioral management is used to represent the structured environment that is systematically applied and usually time-limited interventions, which are carried out by home care staff in the vigilance of a professionally expert in this area. Behavior management is used as an intervention program for those patients, who live in various types of residential settings, but this is associated with the severity level of dementia in individuals. The largest and the most complex duration of the intervention and its study period is up to 12 weeks.<sup>11</sup>

Behavior management may be used to crease the level of depression in people with dementia. Various studies suggest that the decline this therapy is useful for those patients

who have repetitive verbalizations, management of eating behaviors and management of aggression and they have a very positive effect of this therapy on their behavior and well-being.

Multi-dimensional behavior management programs may give more effective results than interventions of individual in the improvement of the behavior as well as the well-being of demented people. This method cannot be suggested for other symptoms of dementia because there is a shortage of reliable evidences. More studies should be done in this area for reliability increment and should be varied according to the severity of dementia.<sup>12</sup>

### Caregiver Intervention Programs

This form of intervention expands from the simplest reassurance to the extremely complex multi-dimensional interaction with the demented people, including a caregiver residential program. Present guidelines assessed only organized caregiver intervention programs. This treatment has minimal and time-limited clinical impact on the patients, but those have great benefit of this program who are suffering from severe dementia. Comprehensive and professional training of interventions is required for caregivers for effective results to treat dementia patients.<sup>13</sup>

### Cognitive Stimulation

Recreational activities help to create cognitive stimulation. It can be done formally through a memory provoking program, conversational fluency and problem-solving activities through spaced retrieval method including face name training. A positive clinical effect is produced through formal cognitive stimulation in dementia patients. The training of cognitive stimulation can be started at home by a caregiver. The risk level for the patients can be declined with minimal training or education of the carer.<sup>14</sup>

### Environmental Design

This type of designing includes residential unit design, such as corridor configuration to reduce restlessness, anxiety and disorientation in people with dementia who are institutionalized. It has been reported that people with dementia experience rapid impairment of memory and cognitive decline. It is needed to have such an environment that increases orientation. A number of studies have reported that positive changes in the environment can affect the patients positively who are suffering from dementia. This method usually measures the problem behaviors with activities of daily livings (ADLs) and cognitive and social activities. This type of intervention includes simple modifications in the physical environment, e.g. signage and homelike environments, ADLs, behavior, and orientation. Small size groups living in, had a positive therapeutic effect.<sup>15,16</sup>

### Multisensory Stimulation (MSS) and Combined Therapies

Studies recommend that through MSS several sensory modalities can be gained rather than single-sense stimulation in dementia. In this approach various equipments are used, e.g. relaxing music, lighting effects, massage cushions, tactile surfaces, recorded sounds, and fragrances in the creation of a multisensory stimulating environment. Some other studies have observed the use of combinations of aromatherapy with essential oils like lavender and lemon balm, massage, and music.<sup>17</sup>

#### Aroma therapy

Aromatherapy is one of the major randomized controlled trials in the intervention of people with dementia. It has been observed that *Melissa officinalis* (lemon balm) have a positive impact on agitation even in the case of continued receiving of neuroleptic medication by the patient, but the possibility of dose adjustments during the study period, can create the confounding the results. *Lavendula officinalis* (lavender oil) has not proved much efficient to reduce the associated symptoms of dementia in the patient. The aromatherapy should be used after the consultation of qualified aroma-therapist.

#### Light therapy

Irregularity of sleep in demented people can be much distressing and troublesome for carers. This is due to the biological changes in the brain which disturb the normal circadian rhythm and sleep/wake cycle. With the help of bright light, production of melatonin is affected, which may decrease these problems. This is an intensive labor program, and sometimes it faces the problems regarding the control of studies of staff interaction and it maintains blinding also. This therapy is not suggested for the intervention of cognitive impairment, agitation, and sleep disturbance in people with dementia.<sup>18,19</sup>

#### Music therapy

Various studies suggested that exposure to music, suitable to the individual's choice, can decrease agitation but not the aggressive behavior in demented people. It is difficult to ensure whether the desired effects seen are the result is due to music therapy itself or because of other factors, e.g. researcher's presence. Music therapy is convenient to imply, but further researches are needed to determine its beneficial aspect for a person with dementia.<sup>20</sup>

### MSS

MSS is difficult to imply and not easy to tolerate by everyone. The variations in severity level of dementia between the intervention and targeted groups in studies decrease the reliability and validity of conclusions which are obtained. Multisensory environments help to individuals to expose less confusion and to talk more spontaneously with normal length sentences.

- MSS may be a clinically useful intervention for people with moderate dementia.
- This therapy is not suggested for relief of neuropsychiatric symptoms in moderate to severe demented people.<sup>21,22</sup>

#### Physical activities

Exercise programs for dementia patients includes improvements in walking, ambulatory status, endurance and urinary continence, but lack of reliable evidence for its support. Various meta-analysis studies showed that the exercise has a statistically significant positive outcome in people who aged over 65 and have dementia and cognitive impairment. An amalgamation of structured exercise and conversation may help to maintain mobility in people with dementia.<sup>23</sup>

#### Reality orientation therapy (ROT)

ROT is one of the major approaches in psychosocial intervention in the care of people with dementia. The aim of ROT is to re-orientate the patient through continuous stimulation and the repetitive orientation toward the environment. This may be formally done in a daily group session, or informally in the way of communicating with individual with involving the orientation to place, time, and the person in the whole day (24 h methods). ROT should be carried out by a skilled practitioner with those people who are disorientated in time, place and person, on an individualized basis.<sup>24,25</sup>

#### Recreational activities

Recreational activities help to engage the people with dementia in meaningful activities and frequently used as a way of enhancing the individual's need for communication, sense of identity, self-esteem, and productivity. This approach used a number of activities including self-expression in the form of drawing, arts and crafts, music, cooking, games and interacting with pets. Recreational activities are helpful to people with dementia to enhance their quality of life and well-being.<sup>25,26</sup>

#### Simulated presence

The purpose of this therapy is to keep the environment as familiar as possible for the patient with dementia to reduce his anxiety and distress. It includes the making of a recording of a familiar person to the patient and playing it into the front of the patient. The content of the can be varied according to the interests of the individual patient concerned. Simulated presence therapy was associated with improved alertness for nursing home residents, but no clinical benefits are provided compared to a placebo tape recording.<sup>25,27</sup>

### Validation therapy

Validation therapy is used to communicate with elderly people who are disorientated; it involves acknowledging and supporting the feelings in of the patients, whatever time and place are seem real to them, even without corresponding with their “here and now” reality. This is different from ROT, whose aim is to draw the person in the present reality. The main benefit of validation therapy is the restoration of self-worth and minimization of the degree of patients’ withdrawal from outside the world. It promotes the communication and interaction of the patient with other people and helps to reduce the stress and anxiety stimulation. It helps them to resolve the unfinished tasks of their lives and facilitates the independent living for as long as possible.<sup>28-30</sup>

## PHARMACOLOGICAL TREATMENT

The suggestions given in this field are based upon an interpretation of the available evidence to examine clinical potentials of this approach. Cost effectiveness has not been included in it. The core features of this illness are reducing cognitive and dexterous motor ability. A large number of problems are associated with it, which often occur, but not in uniform way. These kinds of problems are referred as behavioral and psychological symptoms of dementias (BPSD), which can develop a

severe distress for the patients, as well as their carers, also. The presentation of the following symptoms such as irritability, agitation, sleep disturbance, hallucinations, delusions or aggression may lead the patient to the hospital or institutional care.<sup>1</sup>

These symptoms are associated traditionally with the use of antipsychotic, antidepressants or anxiolytic drug or medication. The problematic behavior of patients may also be influenced by the use of acetylcholinesterase drugs (Tables 1 and 2).

### Vascular Dementia or Stroke Related Dementia

Brief evidence has been found associated with the treatment of behavioral and psychological disorder in vascular dementia or stroke-related dementia. Some drugs such as cholinesterase inhibitors (galantamine; rivastigmine; donepezil) and memantine are not licensed to be used for the treatment of vascular dementia. It is important for the prescribers to follow the guidelines to use drugs with extreme cautions for AD, keeping the established increased cerebrovascular risk (i.e., antipsychotics) in mind.<sup>32</sup>

### Other BPSD and Other Dementias (e.g. Fronto-temporal Lobe Dementia)

The treatment of another BPSD has a little evidence base or for the curing of common BPSD in other forms of

**Table 1: Index to core and associated symptoms and pharmacological interventions<sup>31,32</sup>**

Key symptom	First line	Evidence type	Second line	Evidence type
Depression	Sertraline, citalopram	2-3+£	Mirtazapine	3
Psychosis	Risperidone	1	Olanzapine, quetiapine, memantine, haloperidol	2
Aggression	Risperidone	1	Olanzapine, quetiapine, memantine haloperidol	2
Moderate agitation/anxiety	Citalopram	3	Trazodone, mirtazapine	4
Severe agitation/anxiety	Risperidone	1	Olanzapine, or memantine±short term benzodiazepine if atypical inappropriate	1,2
Poor sleep	Temazepam, zopiclone	3+£	Clomethiazole	

**Table 2: DLB or Parkinsons disease dementia<sup>7,31</sup>**

DLB or Parkinson's disease dementia key symptom	First line PDD	First line LBD	Evidence type	Second line PDD	Second line LBD	Evidence type
Depression	Citalopram		4+£	Sertraline	4	
Psychosis	Quetiapine	Rivastigmine; donepezil galantamine	3	Clozapine, rivastigmine	Memantine	2-3
Aggression	Quetiapine	Rivastigmine donepezil; galantamine	3	Rivastigmine	Memantine	3
Moderate agitation/anxiety	Citalopram	3+£	*Rivastigmine	Rivastigmine donepezil S; galantamin		2-3
Severe agitation/anxiety	Quetiapine	Rivastigmine donepezil galantamine	3	Rivastigmine±short term benzodiazepine	Memantine±short term benzodiazepine	3
Poor sleep	Temazepam, zopiclone		3+£	Clomethiazole	3	
REM sleep behaviour (nightmares, hyperactivity)	Clonazepam			3		

PDD: Parkinson's disease dementia, LBD: Dementia with Lewy bodies, REM: Rapid Eye Movement



**Table 3: Drug dose guidelines for use of antipsychotics in dementia<sup>32</sup>**

Drug dose guidelines for use of antipsychotics in dementia antipsychotic	Starting dose
Risperidone	250 µg twice daily
Olanzapine	2.5 mg daily
Quetiapine	25 mg daily
Haloperidol	500 µg twice daily

dementias. Hence that is it essential to take specialist advice for the treatment of other BPSD I (Table 3).<sup>31</sup>

## CONCLUSION

The most common problems in a dementia patient are behaviour problems, which require a physician's consultancy and/or hospitalization. They are multifactorial in nature; therefore, its management should also be multifaceted. First of all non-pharmacological interventions should be used for behavior system management, but if non-pharmacological interventions are not much competent then pharmacological intervention should be tried later. The use of a multidisciplinary approach is always worthy, because the root causes of behavioral problems are a mixture of organic, environmental, behavior and psychological factors. A good behavioral management system is not only valuable for a person but may also proceed to minimal change in environment and put less burden of stress on caregivers. If a differential diagnosis has been obtained once, and the behavioral problem elicited, then worked up conducted through both pharmacological and non-pharmacological interventions. In this way, both forms of intervention are important for better behavior management, but the non-pharmacological should always be the first step of the treatment program.

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# Iliopsoas Abscess: A Clinical Dilemma – Case Report

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## Abstract

Iliopsoas abscess is an uncommon condition, which can present with vague clinical features. Its subtle onset and uncommon characteristic leads to diagnostic delay thereby increasing the morbidity and mortality. Literature usually classifies iliacus abscess and psoas abscess as a single entity. Iliacus muscle is a separate structural entity surrounded by its own fascia though having combined function with the psoas muscle hence clubbed together functionally. Iliacus abscess is more morbid than psoas abscess. Tubercular iliopsoas abscess is extremely rare to be found without spinal affection. Here, we present a case of 35-year-old female presenting with 7 days history of pain in left iliac fossa with restriction of left hip joint developing into a fixed flexion deformity, thereby creating a clinical dilemma of synovitis. Magnetic resonance imaging report revealed iliopsoas abscess without involvement of the spine. Other conditions which may mimic iliopsoas abscess are septic hip, osteomyelitis, and appendicular abscess.

**Keywords:** Iliacus muscles, Iliopsoas abscess, Tuberculosis

## INTRODUCTION

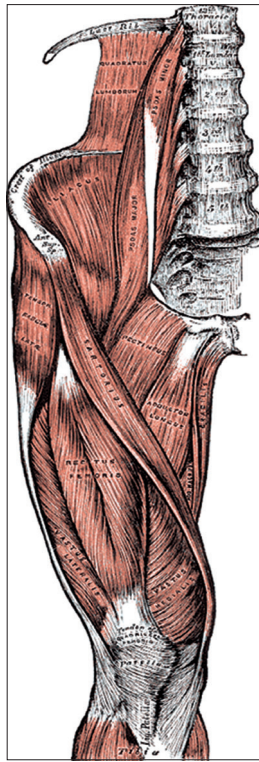
The iliopsoas compartment is an extraperitoneal space in which the psoas and iliacus muscles are situated. The psoas muscle is a long fusiform muscle placed on the side of the lumbar region of vertebral column and brim of lesser pelvis. The muscle proceeds downwards across the brim of lesser pelvis and decreases in size passing between the inguinal ligament and front of the capsule of the hip joint and ends in tendon. The tendon receives nearly the whole of fibres of iliacus muscle and is inserted into lesser trochanter of femur hence at times psoas and iliacus muscle are referred as a single muscle named iliopsoas (Figure 1).<sup>1</sup>

These muscles have a rich vascular supply that is believed to predispose it to hematogenous spread from the site of occult infection.<sup>2</sup> Tubercular psoas abscess originates from the spine and rarely from the digestive, urological or genital tuberculosis (TB). Primary iliopsoas abscess occurs probably, as a result, of hematogenous spread of an infectious process from an occult source in the body. Crohn's disease is the commonest cause of secondary iliopsoas abscess<sup>3</sup> in the western world.

Tuberculousiliacus and iliopsoas abscesses are not easily diagnosed as it showed non-specific symptomatology and associated with late diagnosis.<sup>4</sup> The classical triad consisting of fever, back pain and limp is present in only 30% of the patients with iliopsoas abscess<sup>5</sup> thereby becoming a diagnostic dilemma.

## CASE REPORT

A 35-year-old female presented with a complaint of pain in left iliac fossa with difficulty in movement of left hip joint gradually developing fixed flexion deformity of left lower limb. There was no history of trauma. On physical examination, there was tenderness over the anterior aspect of the hip joint and left iliac fossa. The left limb was in the attitude of flexion of 30°, restricted extension of left hip joint and also abduction and adduction painful at 30° and 20° with severe restriction of internal rotation of left hip joint. There was no abnormal finding on per abdominal examinations. The initial ultrasonography (USG) abdomen and left iliac fossa findings were reported as normal. The initial diagnosis based on clinical examination and USG was acute synovitis of left hip. Patient was put on intravenous



**Figure 1: Origin and insertion of iliacus and psoas muscles**

analgesics and muscle relaxants, but patient did not get any relief.

Laboratory investigations showed Hb 10.5 g%, white blood cells (WBC) 19,700, Ne 65%, Eo 14%, Ly 16%, Mo 5%, erythrocyte sedimentation rate 109. Serum urea and serum creatinine were within normal range. X-ray chest was normal.

The patient was then subjected to magnetic resonance imaging (MRI) after 5 days as she did not get relieved on traction and intravenous analgesics.

### MRI Report

The left iliacus muscle appears bulky due to edema. Multiple areas showing partial liquefaction are scattered within the approximate size of the “collection” is 9.5 cm craniocaudally and 6.0 cm × 3.7 cm in maximum transverse dimension. Inflammation is also seen within the inferior portion of the psoas muscle without vertebral erosions. The obturator internus muscle also appears bulky and diffusely edematous. Enlarged lymph nodes in the pelvis and inguinal region bilaterally and also seen along the lateral abdominal muscles. Edema of the adjoining left obturator and femoral nerves (Figures 2 and 3).

The patients WBC count rose to 23,000. She was then subjected to surgical drainage in view of increasing sepsis and iliopsoas abscess was drained. Iliac crest



**Figure 2: MRI T1 axial cut of pelvis showing iliopsoas abscess**

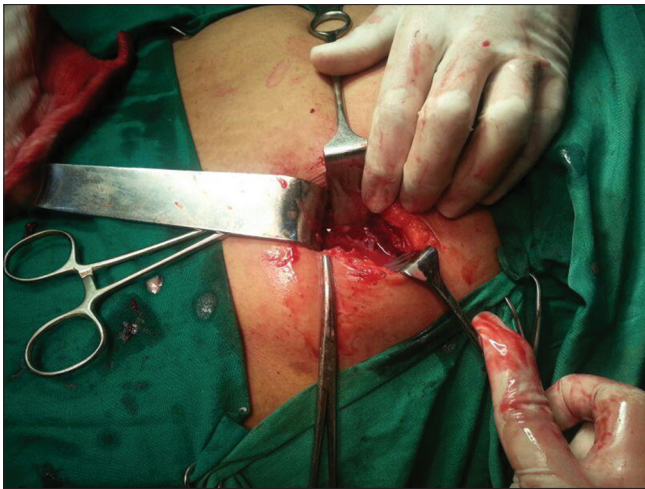


**Figure 3: MRI T2 axial cut showing oedema of adjoining obturator and femoral nerves along with the abscess**

apophyseal-splitting incision was done, and this made easy and direct approach toward the iliopsoas muscle and abscess (Figure 4). Thick pus approximately 100 cc drained out and necrotic tissue debrided. The pus sent for bacteriological culture and sensitivity and abscess wall for histopathology. Pus culture is showing *Staphylococcus aureus* and histopathology report revealing the tuberculous inflammation. Patient then put on antibiotics and on anti-tubercular drugs (isoniazide, rifampicin, pyrazinamide and ethambutol) to which patient responded remarkably.

### DISCUSSION

TB is endemic in India and Africa.<sup>6</sup> Psoas abscess initially was synonymous with TB of the spine and sacroiliac joint before introduction of streptomycin for the treatment of TB. Psoas abscess is predominant in the western country especially in immune-compromised patient.<sup>7,8</sup> Iliopsoas abscess most commonly originates from osseous source



**Figure 4: Incision and drainage of abscess**

such as spine, ilium, and sacroiliac joint. They rarely arise from pyomyositis, lymphatic spread and puerperal infection.

The average age of patients is between 30 and 40 years, and male patients are affected more than females, at a ratio of 2:1.<sup>9</sup>

Iliopsoas abscess may initially present with signs and symptoms in the buttock, hip or thigh. Such signs and symptoms may be obscure, non-specific and misleading.<sup>10</sup> In the case of psoas involvement, there is flexion of the hip with painful range of movement thus misleading the diagnosis from abdominal or a pelvic source of abscess.<sup>11</sup>

The most common organism implicated in ilio-psoas abscess is *S. aureus*.<sup>12,13</sup> Another organism has also been isolated.<sup>14,15</sup> The other causative organisms include *Escherichia coli*, *Mycobacterium TB*, *Proteus*, *Pasturella multocida*, *Bacteroides*, *Clostridium*, *Yersinia enterocolitica*, *Klebsiella*, methicilin resistant *S. aureus*, *Salmonella*, *Mycobacterium kansasii*, *Mycobacterium xenopi*.

Computed tomography (CT) is a method of choice for abscess detection. MRI is also of important to reach a diagnosis. Only 60% can be diagnosed by USG as compared to CT scan accuracy which is around 80-100%.<sup>16,17</sup>

CT-scan and USG allow percutaneous needle aspiration and drainage and hence both diagnostics and therapeutics. Radical excision of necrosis and tissue along with drainage is the ideal treatment of choice. Per-cutaneous drainage of the iliopsoas abscess is less interventional and at times has been proposed as treatment of choice however there may be possibilities of residual effect for, e.g. osteomyelitis of adjacent bone and muscle weakness due to inadequate treatment. The treatment of tuberculous iliopsoas abscess

should be based on per cutaneous drainage or surgical drainage with broad spectrum antibiotics.

## CONCLUSION

Iliopsoas abscess is a diagnostic dilemma due to atypical signs and symptoms of the lower extremity. The classic symptoms of iliopsoas abscess: Fever, flank pain and limitation of hip movement, are, in fact, atypical and have presented in only 30% of patient.<sup>18</sup> Once a diagnosis of psoas is established successful treatment should include surgical drainage and excision of all necrotic tissue. In our case, there were no classical symptoms of inflammation but the patient presented with the atypical symptoms and signs. With the help of imaging techniques and the pus and histopathology report, we have reached the diagnosis of tubercular iliopsoas abscess with suppurative inflammation. Patient with chronic backache to consider for CT/MRI evaluation to rule-out musculo-skeletal TB. CT-scan is the gold standard in evaluating and diagnosing the iliopsoas abscess.<sup>19</sup> Awareness of disease entity, thorough physical examination and imaging studies such as USG, CT-scan and MRI should be done to reach an accurate diagnosis.

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# Atypical Primary Laryngeal Tuberculosis Presented With Mutational Falsetto: A Rare Case Report

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## Abstract

Tuberculosis is the most common granulomatous disease of the larynx, but still constitutes <1% of all cases of extra pulmonary tuberculosis. We report a case of 17-year-old male who presented with hoarseness of voice for 2 years. On local examination, we diagnosed as puberphonia (mutational falsetto) and voice therapy were advised. Patient reviewed after 3 months with progressive voice change, odynophagia, loss of weight, fever and ring lesion in left face. Video laryngoscopy was done for further examination and laryngeal swab was taken. On examination of the latter by fluorescent light emitting diode microscopy, patient was diagnosed to have typical primary laryngeal tuberculosis and treated with anti-tuberculous regime.

**Keywords:** Laryngeal tuberculosis, Light emitting diode microscopy, Mutational falsetto, Puberphonia

## INTRODUCTION

Tuberculosis is a contagious disease. The main mode of transmission occurs predominantly by droplet infection. It affects lungs primarily but can occur in any organ.<sup>1</sup> Among extra pulmonary tuberculosis, the most common manifestation is the lymphadenitis. In ENT, head and neck tuberculosis is rare in which the most common site is larynx excluding cervical lymphadenitis.<sup>2</sup> Tuberculosis is considered one of the most common granulomatous diseases of the larynx, but still constitutes <1% of all cases of extra pulmonary tuberculosis.<sup>3</sup> The diagnosis of laryngeal tuberculosis is challenging, as its presentation varies. Mutational falsetto is a functional voice disorder, being a failure to change from the high-pitched voice of preadolescence to the low-pitched voice of adolescence and adulthood in male.<sup>4</sup> We report a case of atypical primary laryngeal tuberculosis, which presented with mutational falsetto.

## CASE REPORT

A 17-year-old male patient came to the ENT outpatient department with the history of hoarseness of voice for 2 years which were high-pitched. ENT examination was

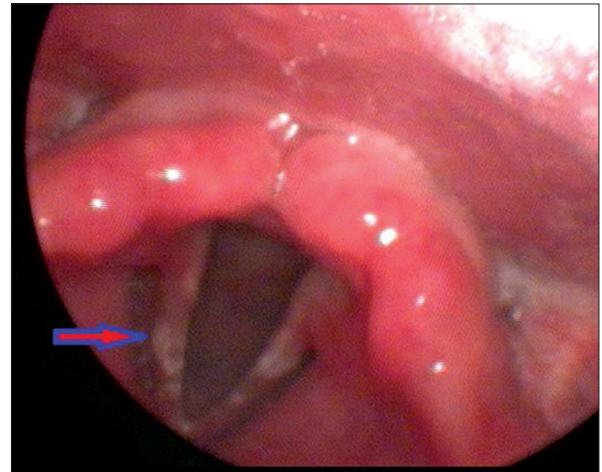
done. Video laryngoscopy using 45° rigid endoscope showed hooding of epiglottis (Figure 1), presence of phonatory gap during adduction (Figure 2) and normal-appearing vocal cords. Patient underwent voice assessment and speech profile showed high pitched voice, inadequate loudness, mild hoarseness and presence of pitch breaks. Maximum phonation duration shows 'a'-5 s, 'I'-4 s, 'u'-4 s, 'z'-3 s. Hence, the patient was diagnosed as having puberphonia and was advised speech therapy. After 3 months, patient presented with progressive hoarseness of voice, odynophagia, fever, loss of weight and appetite and ring lesion in the left side of the face for 1 month duration. On local examination of the larynx, video laryngoscopy showed hooding of epiglottis with granulations, multiple bilateral ulcerations (mouse nibbled appearance) (Figure 3), bowing of true vocal cords and edema of the arytenoids and aryepiglottic folds (Figure 4). Dermatology opinion was obtained for lesion in face and impression was tinea infection (Figure 5). Mantoux test was positive (16 mm) (Figure 6) and sputum for acid-fast bacillus (AFB) by routine Ziehl-Neelsen method was negative. Basic laboratory tests including complete haemogram, blood sugar, renal function tests and liver function tests were normal except for elevated erythrocyte sedimentation rate (ESR) and lymphocytosis (Table 1). Plain film radiography of the chest posteroanterior view

was normal (Figure 7). A swab was taken from larynx with the help of 45° endoscope and examined under fluorescent light emitting diode (LED) microscope and tuberculous bacilli were clearly seen (Figure 8). Sputum culture done and was positive for *Mycobacterium tuberculosis*. Finally, the case was diagnosed as atypical

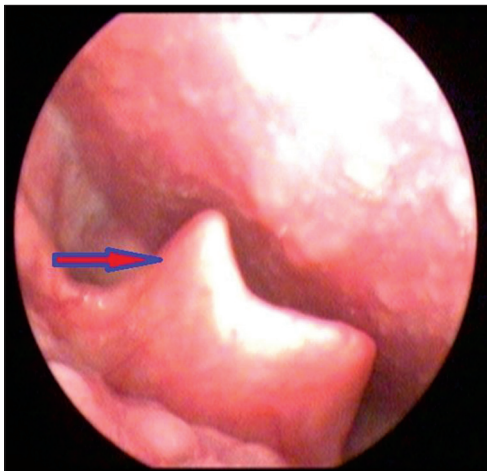
primary laryngeal tuberculosis. The patient was treated with anti-tuberculous regimen, topical clotrimazole cream for facial lesion and advised to continue speech therapy for 6 months. His family members were screened for tuberculosis contact.

**Table 1: His investigations are as follows**

Hemoglobin	12 g
Total count	6200 cells/mm <sup>3</sup>
Differential count	P-42%, I-56%, e-2%
Erythrocyte sedimentation rate	66 mm/h
Platelet count	2.9 lakh/mm <sup>3</sup>
Random blood sugar	90 mg
Urea	21 mg
Creatinine	0.6 mg
Total bilirubin	0.9 mg
Direct bilirubin	0.6 mg
Aspartate transaminase	19 U
Alanine transaminase	23 U
Alkaline phosphatase	110 U
Serum albumin	4 g%
Total protein	7 g



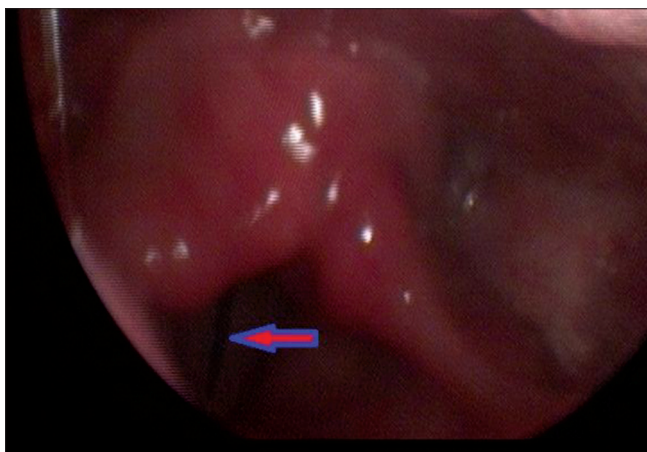
**Figure 3: Mouse nibbled appearance**



**Figure 1: Hooded epiglottis**



**Figure 4: Arytenoids and aryepiglottic fold edematous**



**Figure 2: Phonatory gap present**



**Figure 5: Ring lesion**



## RESULTS

On the follow-up of the patient after 5 months, laryngeal lesions (Figure 9) and facial lesion (Figure 10) cleared up completely, repeat laryngeal swab examined under

LED microscope was negative for tuberculous bacilli (Figure 11) and voice became normal. The mode of presentation of typical primary laryngeal tuberculosis varies and in this case, it presented with mutational falsetto.



Figure 6: Moutaux test positive



Figure 9: Normal appearance of larynx



Figure 7: Chest radiography shows normal study



Figure 10: Ring lesion disappeared

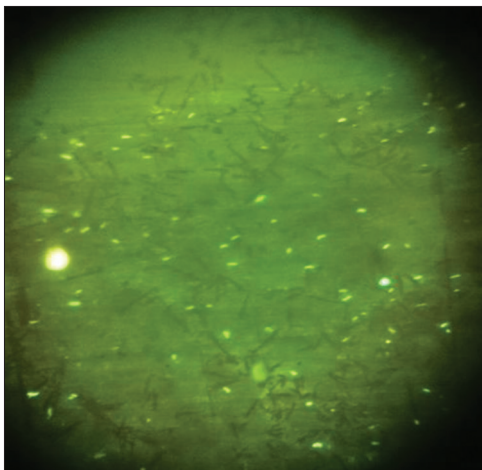


Figure 8: LED microscope shows presence of tuberculous bacillus

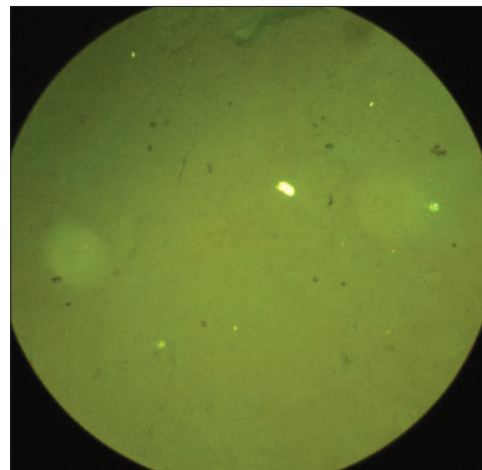


Figure 11: LED microscope shows negative for tuberculous bacillus



## DISCUSSION

The persistence of adolescent voice even after puberty in the absence of an organic cause is known as puberphonia. This condition is commonly seen in males. The patient has an unusually high-pitched voice persisting beyond puberty. This is uncommon in females because laryngeal growth spurt occurs commonly only in males.<sup>5</sup> Voice therapy is a behavioral method for changing the manner of voice production. Furthermore, the therapeutic techniques used in voice therapy may enhance wound healing following vocal fold injury. Voice therapy is an effective and appropriate method of treatment either as sole therapy for voice disorders or in conjunction with other treatment modalities.<sup>6</sup> The characteristics of laryngeal tuberculosis have changed over the years, and it has become a challenge for otolaryngologists to distinguish this disease from others. The laryngeal anatomy of individuals presenting with mutational falsetto appears to be normal, but in our patient it was not so.

The diagnosis of tuberculosis is suggested by a positive mantoux test, sputum for AFB, caseating granulomas on histopathological examination, classical radiological features, elevated ESR and positive AFB culture. However, we confirmed the diagnosis by using laryngeal swab examined under fluorescent LED microscope and AFB culture as confirmation is by identification of *M. tuberculosis*.<sup>7</sup> In LED microscope, fluorescent dye named auramine phenol is used as the primary stain and 0.1% potassium permanganate is used for counterstaining. LED microscopy provides a reliable alternative to conventional methods and has many favorable attributes that facilitate improved, decentralized, diagnostic services.<sup>8</sup>

Treatment includes direct observed treatment short course therapy according to the Revised National Tuberculosis Program Guidelines. Our patient, a newly diagnosed case of extra pulmonary tuberculosis, was treated under Category I regimen. It includes treatment with four drugs intensive phase for 2 months with isoniazid 300 mg, rifampicin 600 mg, pyrazinamide 1500 mg and ethambutol 1000 mg, followed by 4 months of the continuation phase

with isoniazid 300 mg and rifampicin 600 mg thrice a week. Although it seems difficult to detect laryngeal tuberculosis early, response to anti-tuberculous therapy is excellent in most of the patients.<sup>9</sup> Tuberculosis should be considered in the differential diagnosis of patients who present with any form of laryngeal lesion. Prompt diagnosis is important as a delay poses a significant public health risk.<sup>10</sup>

## CONCLUSION

Laryngeal tuberculosis is still a frequent complication of pulmonary tuberculosis. However, there can be primary laryngeal lesions without any pulmonary involvement, and this patient atypically seems to manifest as puberphonia that is very difficult to diagnose.

The successful management of typical laryngeal tuberculous patients, lies in a high degree of clinical suspicion, prompt diagnosis and early intervention by initiation of appropriate anti-tuberculous therapy.

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# Skin Lesions Still the “Sine Qua Non” for Diagnosing Erythema Multiforme? - A Case Report with Critical Literature Review

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## Abstract

Erythema multiforme (EM) is an uncommon, acute inflammatory vesiculobullous disorder affecting the skin and/or mucous membranes. The oral variant of this condition is even more uncommon. Here we present a case of herpes-associated EM affecting the oral cavity where the skin lesions, which were considered the “sine qua non” for EM diagnosis, were absent. The case was promptly and precisely diagnosed and treated using a standardized regime of systemic corticosteroid therapy with supportive care to which he responded well and continues to be disease-free at 1 year follow-up.

**Keywords:** Erythema multiforme minor, Herpes associated erythema multiforme, Oral erythema multiforme

## INTRODUCTION

Although first recognized in early 19<sup>th</sup> century, it was not until 1860 that Ferdinand von Hebra coined the term “erythema multiforme (EM)” to denote this disease.<sup>1</sup> It is basically a hypersensitivity reaction believed to be a sequelae of a cytotoxic immunologic attack on keratinocytes expressing non-self antigens, which are primarily caused by microbes (viruses), drugs or food additives. When herpes simplex virus (HSV) infection is implicated, the diagnosis is herpes-associated EM (HAEM). There may be a genetic predisposition to EM. Human leukocyte antigen DQ3 has been proven to be especially related to recurrent EM and maybe a helpful marker to distinguish HAEM from other diseases with EM-like lesions.<sup>2-6</sup> EM typically affects teenagers, and young adults (20-40 years).<sup>7,8</sup> It affects males more than females in a ratio of 3:2.<sup>9</sup> Here we share a case of oral EM without skin involvement presenting as acute onset stomatitis which can be a diagnostic dilemma to an oral physician.

## CASE REPORT

A 32-year-old male reported to the dental clinic complaining of extensive oral ulcerations, pain, inability to eat and burning sensation since 3 days. There was a history of sudden onset of fluid-filled blisters in the mouth, rapidly increasing in number and size, spontaneously bursting thereafter.

Patient was afebrile with no lymphadenopathy present. Odynophagia and dysarthria were present. Cracking and encrustations were seen on the edematous lips. Intra-orally multiple irregular, coalescing bullae ~5-8 mm in size were seen involving labial mucosa (Figure 1). Bilaterally buccal mucosae showed large, irregular ulcerations with sloughing suggestive of ruptured bullae (Figure 2). Soft palatal involvement was also seen (Figure 3). Tongue was coated and showed focal areas of erosions. Nikolsky's sign was absent. No “target lesions” were seen on the skin.

There was history suggestive of herpes labialis 2 weeks before the episode. Based on this along with the history, a provisional diagnosis of HAEM oral variant was made. Incisional biopsy prove non-specific as expected showing focal ulcerations with dense sub-epithelial infiltration especially in the peri-vascular areas (Figure 4). Direct immunofluorescence showed non-specific deposits of IgG, IgM and C3 at basement membrane and peri-vascular areas. A herpes culture taken from the lip erosions was negative. However, serology for HSV came

out to be positive for IgG confirming the diagnosis of HAEM.

The patient weighed 62 kg and was put on a course of systemic corticosteroids (tablet prednisone 20 mg BD for 7 days which was quickly tapered off and stopped in 2 weeks), capsule erythromycin estolate 500 mg TID for 3 days and topical anesthetic agent (lignocaine). Careful oral hygiene and soft diet were advised to the patient. The patient was able to eat and drink pain-free within 48 h. A follow-up oral examination at 7 days showed complete healing of the oral ulcerations (Figures 5-7). 1 year after the episode, the patient continues to be a disease free.

## DISCUSSION

The presentation of EM ranges from the self-limited, mild form (EM minor) to progressive, and aggressive form like EM major Steven Johnson syndrome and toxic epidermal necrolysis<sup>10</sup> (Table 1).



Figure 1: Pre-treatment-irregular bullae involving labial mucosa



Figure 2: Pre-treatment-Buccal mucosae showing extensive ulcerations with sloughing

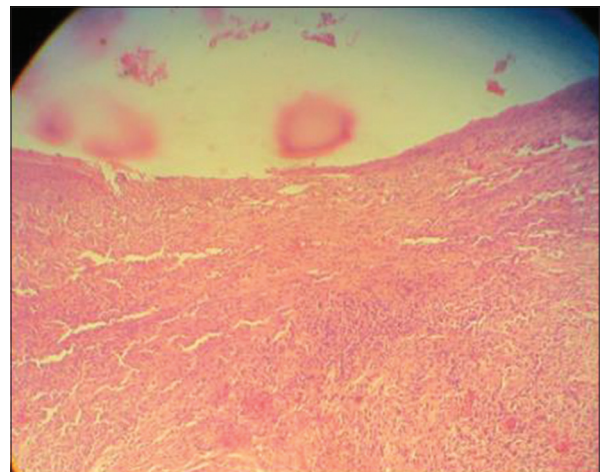


Figure 4: Photomicrograph at low power showing focal ulceration and dense subepithelial and perivascular infiltration



Figure 3: Pre-treatment-soft palate involved



Figure 5: Post-treatment-healed lesions of the labial mucosa





**Figure 6: Post-treatment-healed buccal mucosa lesions**



**Figure 7: Post-treatment-healed soft palate lesions**

Diagnosis of EM, tends to be centered on dermatologic lesions of the extremities, with mouth ulcers regarded as a secondary finding.<sup>11</sup> The concept of pure oral EM is controversial and not universally accepted since some dermatologists believe that the characteristic appearance and distribution of skin lesions are the “sine qua non” for its diagnosis.<sup>12</sup> Kenett<sup>13</sup> (1968) described EM affecting the oral cavity. Since then, many reports have been published describing EM sans skin lesions. It has been suggested that a third category, i.e., the oral variant of EM be incorporated into the current classification.<sup>14,15</sup> The diagnosis of oral EM is one of exclusion.<sup>4</sup>

The differential diagnosis for the case presented here included pemphigus vulgaris, cicatricial pemphigoid, bullous lichen planus, major oral aphthous ulcerations, HSV infection and EM. The biopsy helped rule out the first three. Also, our case was acute in onset in contrast to a chronic nature of these conditions. It would be clinically challenging to distinguish major aphthae from EM, if EM occurs sans the pathognomic target lesions. Here, histopathological and direct immunofluorescence findings were found compatible with the diagnosis of EM. Furthermore, there was a history of preceding HSV infection. But the lip erosions were negative for HSV culture. Hence, the question of herpetic gingivostomatitis (primary/secondary) was nullified. The clues mentioned

**Table 1: Differential features of erythema multiforme minor, erythema multiforme major, Stevens-Johnson syndrome and toxic epidermal necrolysis**

Condition	Pattern of skin lesion	Body surface area with epidermal detachment (%)
EM minor	Typical target lesions, raised atypical target lesions, minimal mucous membrane involvement and when present at only 1 site (most commonly the mouth). Oral lesions; mild to severe erythema, erosions and ulcers	<10
EM major	Cutaneous lesions and at least 2 mucosal sites (typically oral mucosa) affected. Symmetrically distributed typical target lesions or atypical, raised target lesions or both. Oral lesions usually widespread and severe	<10
SJS	Main difference from EM major is based on the location of lesions and the presence of systemic symptoms primarily atypical flat target lesions and macules rather than classic target lesions. Generally widespread rather than involving only the acral areas. Multiple mucosal sites involved, with scarring of the mucosal lesions. Prodromal flu-like systemic symptoms also common	<10
Toxic epidermal necrolysis	No typical targets, flat atypical targets; begins with severe mucosal erosions and progresses to diffuse, generalized detachment of the epidermis	>10

EM: Erythema multiforme, SJS: Stevens-Johnson syndrome

hereby would help an oral physician unerringly to arrive at the diagnosis of oral EM.

Spontaneous healing of EM can be slow, up to 2-3 weeks in minor and up to 6 weeks in major.<sup>2</sup> Treatment is thus indicated but controversial.<sup>16</sup> Precipitating factors should be dealt with immediately. The use of corticosteroids is controversial.<sup>2</sup> There are several arguments for and against the use of systemic corticosteroid therapy for managing this spectrum of diseases.<sup>17</sup> Investigators against it lay emphasis on the lowered immunity leading to increased morbidity and mortality.<sup>7,18,19</sup> Advocates for their use suggest that early administration in the course of the disease is essential.<sup>20,21</sup> A consensus regarding the standard treatment for EM is yet to be reached. A randomized control trial maybe required without overlooking the ethical obligations.

In our case, since the patient was culture negative at the time of presentation and had reported relatively early on, a systemic corticosteroid regime was adopted with dosing as per literature (0.5-1.0 mg/kg/day).<sup>22</sup> Also supportive care was provided alongside. We thereby conclude that with careful diagnosis and case selection, the management



of EM will not be a difficult task, even for general dental practitioner.

## CONCLUSION

The idea of classic textbook “target lesions” of EM may hamper the oral physician in considering the diagnosis of oral EM in acute onset stomatitis. This condition of varied etiologies, mimics several other conditions of the oral cavity and can be misleading, therefore, prompt and precise diagnosis is required in order to initiate early management to reduce the associated comorbidity. As more cases of oral EM get reported, this condition will definitely carve its niche into the current spectrum of such diseases. Moreover, by educating the patient about this condition, future recurrences may be prevented.

Differential features of EM minor, EM major, Stevens-Johnson syndrome and toxic epidermal necrolysis.

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# Lujan–Fryns Syndrome and Psychosis

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## Abstract

Lujan–Fryns syndrome is a rare X-linked disorder with a wide range of clinical features. Patients usually present with marfanoid habitus and psychiatric illness. The prevalence and prenatal testing of this disease are unknown. The genetic defect is due to a missense mutation in the MED12 gene. Patients are mostly present with facial dysmorphic features and mild to moderate mental retardation. Patients presenting with symptoms of mental retardation and schizophrenia should also be evaluated for Lujan–Fryns syndrome. There is no specific treatment for Lujan–Fryns syndrome and patients should receive multiple psychological and behavioral counseling for better outcome and prognosis. Genetic counseling is required in patients with positive family history.

**Keywords:** Attention deficit hyperactivity disorder, Autism, Lujan–Fryns syndrome, Marfanoid habitus, Mental retardation, Psychosis

## INTRODUCTION

Lujan–Fryns syndrome is a rare X-linked dominant disorder associated with mild to moderate mental retardation and marfanoid habitus.<sup>1,2</sup> Patients display characteristic marfanoid habitus with tall stature and facial dysmorphisms, mild general hypotonia, and hypernasal voice, and often exhibit behavioral and psychiatric manifestations, namely schizophrenia, and psychosis. The genetic defect is due to a missense mutation in the MED12 gene.<sup>3</sup> However, there is no genetic test available to confirm the diagnosis. Its prevalence is currently unknown. Diagnosis is made on clinical symptoms and presently no definite treatment is available.<sup>4</sup>

Psychopathological and behavioral abnormalities are highly prevalent in those afflicted with Lujan–Fryns syndrome. Studies have shown that 90% of patients exhibit psychopathological manifestations. The most common is a disorder resembling autism. Therefore, psychiatric evaluation should be performed at diagnosis.<sup>5</sup> Although neurobehavioral abnormalities are common in Lujan–Fryns syndrome, some neurobehavioral functioning, including problem-solving, has been retained in certain cases.<sup>6</sup>

Behavioral and psychiatric manifestations include but are not limited to shyness, attention deficit hyperactivity disorder, aggression, emotional instability, psychosis with auditory, and visual hallucinations and schizophrenia. Lujan–Fryns

syndrome should be considered as a differential diagnosis for any male patient who presents with symptoms suggestive of mental retardation and schizophrenia.

## CASE REPORTS

### Case 1

A 13-year-old male patient presented with symptoms of attention deficit hyperactivity disorder. The boy was an only child who was born from a consanguineous marriage. On examination, his height was recorded to be 149 cm (Z Score 1.4) and weight was 26 kg (Z Score 3.5), with normal arm span. Features of facial dysmorphism were present. He had a long face with a small mandible. His nasal bridge was found to be depressed. On examination of the oral cavity, the child was seen to have a high arched palate (Figure 1). Normal ears with maxillary hypoplasia were present.

On psychiatric evaluation, patient had shoddier word reading with mild mental retardation. He was impulsive with easy distractibility and had poor focus for any particular thing. According to history provided by the mother, the child daydreams occasionally and gets really confused with normal day-to-day things. During the evaluation, he uttered inappropriate words with unstrained emotions.

Additional ophthalmological examination was normal. Cardiac examination; echocardiography was found to be



**Figure 1: High arched palate**



**Figure 2: Marfanoid features**

normal, and no abnormalities were found on ultrasound examination. Imaging study of the brain was normal with normal biochemical analysis of the urine and plasma for abnormal amino acids.

## Case 2

A 15-year-old female patient presented with marfanoid features and craniofacial abnormalities. The girl was the oldest of three children, born from a non-consanguineous marriage. Her other siblings did not present with any similar features – And had no positive physical findings or abnormal history. On examination, her height was found to be 152 cm (Z Score 3.3) and weight was 29 kg (Z Score 8.9) with an arm span of 160 cm. On further clinical examination, she was seen to have a prominent forehead with an elongated face and a hypo nasal voice. Marfanoid features such as long, slender fingers were present with joint hyper extensibility (Figure 2).

On neuropsychological examination, she was found to have learning disabilities with moderate mental retardation. Upon further profound interviewing, - She admitted to symptoms of psychosis and experienced a hallucination without any formal thought disorders. She showed extreme shyness during the evaluation.

Cardiac evaluation on echocardiography showed a mild degree of ventricle septal defect. Ophthalmological and ultrasound examinations were found to be normal. Brain imaging and urine and plasma amino acids were normal.

## DISCUSSION

Lujan–Fryns syndrome is an uncommon X-linked disorder related to varying degrees of mental retardation and marfanoid habitus. Patients exhibit physical features

resembling that of Marfan syndrome with tall stature, long, lean extremities, and facial dysmorphisms including long slender face, small mandible, maxillary hypoplasia, large forehead, and high arched palate. It is more common in males and is difficult to diagnose before sexual maturity.<sup>7</sup>

Lujan–Fryns syndrome is associated with various behavioral and psychological abnormalities including attention deficit hyperactivity disorder, shyness, aggressive behavior, autistic spectrum disorder, psychosis, and schizophrenia. In addition, agenesis of the corpus callosum is seen on brain imaging in few cases.<sup>8</sup> Cardiovascular manifestations such as aortic root dilatation and ventricular septal defect have been seen in some cases.<sup>9</sup>

Currently, no treatment is available for the disorder, but patients may require special education and psychiatric counseling. Genetic counseling is also recommended. Diagnosis is made on clinical symptoms.<sup>10</sup>

## CONCLUSION

There is no specific treatment for Lujan–Fryns syndrome and patients should receive multiple psychological and behavioral counseling for better outcome and prognosis. Genetic counseling is required in patients with positive family history.

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# Hemifacial Microsomia Associated with Facial Palsy and Oculo-Auricular Malformation: A Rare Case Report

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## Abstract

Hemifacial microsomia (HFM) is the most frequently encountered form of isolated facial asymmetry. It is a congenital facial deformity involving the structures of the first and second pharyngeal arches: Maxilla, mandible, external and middle ear, facial and trigeminal nerves, muscles of mastication, and overlying soft tissue. After cleft lip and palate, HFM is the most common craniofacial malformation. We report a rare case of HFM in association with facial palsy, oculoauricular malformation. The case had variable presentations ranging from the facial asymmetry and ear deformity to the most severe and unusual form with facial nerve paralysis. The article provides a discussion on the etiology, diagnosis and treatment of HFM.

**Keywords:** Facial palsy, Goldenhar syndrome, Hemifacial microsomia

## INTRODUCTION

Hemifacial microsomia (HFM) is a highly heterogeneous condition with an estimated rate of 1 in 5600-20,000 births,<sup>1</sup> perhaps making it the most significant asymmetric craniofacial disorder. Gorlin used the term HFM to describe a spectrum of abnormalities such as macrostomia, unilateral microtia, and underdeveloped mandibular ramus, and condyle. These patients have differences in the size and shape of facial structures between the right and left sides of the face (facial asymmetry). Patients with HFM show different clinical manifestations thus identified by various nomenclature such as Goldenhar syndrome, oculo-auriculo-vertebral spectrum, facio-auriculo-vertebral dysplasia, and first and second branchial arch syndrome. Wide spectrum of anomalies associated with HFM involves one or both ears, eyes, facial nerve, mandibular nerve, soft-tissue and vertebral abnormalities. Mild-to-severe ear findings may involve an underdeveloped or absent external ear (microtia, or anotia), growths of skin (skin tags) in front of the ear (preauricular tags), or closed or absent ear canal;

these abnormalities may lead to hearing loss. Sensorineural hearing loss (SNHL) is uncommon in HFM but can be devastating at a time. A rare case of HFM is presented in this article with its characteristics clinical and radiological features that will add a new dimension to the literature.

## CASE REPORT

A 21-year-old male patient reported to Department of Oral Medicine and Radiology complaining of facial asymmetry since birth. No significant positive family history was present. Extra-oral examination revealed underdevelopment of the left side of face involving malformation of ipsilateral eye and ear (Figure 1). Ear examination showed cup shape pinna, low-lying deformity of the pinna also profound SNHL of the left side (Figure 2). The patient was unable to draw back the left corner of his mouth on smiling (Figure 3) and was not able to wrinkle his forehead on the same side (Figure 4). All the features were suggestive of facial nerve paralysis of the left side. Eye examination revealed that the patient was

also unable to close his left eye completely (lagophthalmos) leading to exposure keratitis, iris coloboma of left eye, and when he attempted to close his left eye, the eyeball rotated upwards, demonstrating Bell's sign.

On intraoral examination unilateral cross bite of right side anterior and posterior, rotated right side incisors (Figure 5) and gingival hyperplasia on the palatal aspect of maxillary posterior region of the left side was noted (Figure 6).



Figure 1: Frontal profile of the patient depicting the underdeveloped left side of face



Figure 4: Inability to raise eyebrow of left side



Figure 2: Cup shape pinna, low-lying deformity of pinna



Figure 5: Presence of crossbite on anterior and posterior of right side



Figure 3: Drooping of corner of mouth during smile on left



Figure 6: Gingival hyperplasia

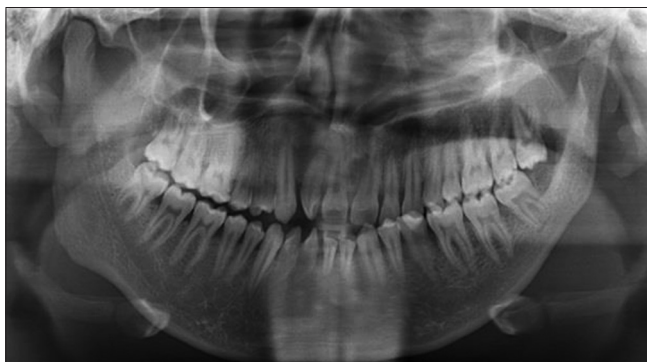
Orthopantomogram revealed a hypoplastic mandible and absence of condylar head and neck, reduced ramus height and width (Figure 7). Lateral cephalometric radiograph depicted increased angle of mandibular ramus & hypoplastic ramus on left side (Figure 8). A frontal skull radiograph (posterior-anterior view) showed the degree of osseous asymmetry of the face (Figure 9). Transpharyngeal view of temporomandibular joint showed absence of condylar head and neck with reduced ramus width on left side (Figure 10). Cone beam computed tomography depicted Facial asymmetry, hypoplastic maxilla and mandible on left side (Figure 11). Cytogenetic investigation revealed normal male karyotype 46 and XY without chromosomal aberration.

## DISCUSSION

Craniofacial microsomia was first described by German physician Carl Ferdinand Von Arlt in 1881.<sup>2</sup> The facial characteristics in HFM typically include underdevelopment of one side of the upper or lower jaw (maxillary or mandibular hypoplasia), which can cause dental problems and difficulties with feeding and speech. In severe cases

of mandibular hypoplasia, breathing may also be affected. HFM is the most common congenital facial anomaly, secondary to facial clefts,<sup>3,4</sup> predominantly seen in males and commonly affects the right side of the face.<sup>5</sup> Goldenhar syndrome (oculo-auriculo-vertebral dysplasia) was described as a variant with vertebral anomalies, epibulbar dermoids, and other anomalies that may also occur in association.

The observations of anatomic variables of HFM are supported by the pathogenic theory of axial mesodermal dysplasia.<sup>6</sup> Findings from a recent ongoing case-control study<sup>7</sup> are consistent with the vascular disruption hypothesis. However, links between HFM risk and other pathogenetic processes such as oxygen free radical generation,<sup>8</sup> maternal diabetes<sup>9</sup> or exposure to teratogens<sup>6</sup> and finally, assisted reproductive technologies have been postulated by many authors.<sup>10</sup> Teratogenic and genetic components have been examined by many investigators. Reports indicate that several teratogenic agents, such as retinoic acid, primidone, and thalidomide, have produced HFM in infants born to pregnant women exposed to those agents. The most useful in clinical practice are the Pruzansky's and Kaban's classifications. In Kaban's<sup>11</sup>



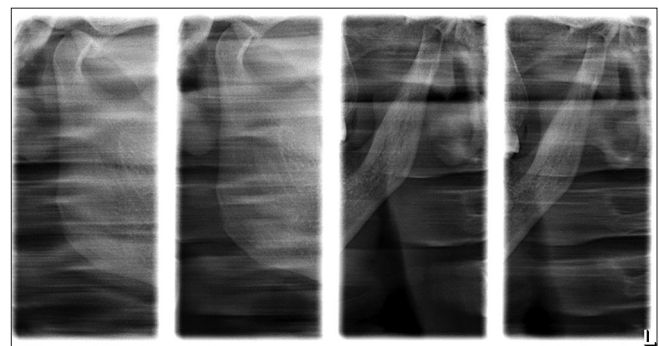
**Figure 7: Orthopantomogram depicts reduced ramus height and absence of condylar head on the left side**



**Figure 8: Lateral cephalometry showing increased angle of mandibular ramus and hypoplastic ramus of left side**

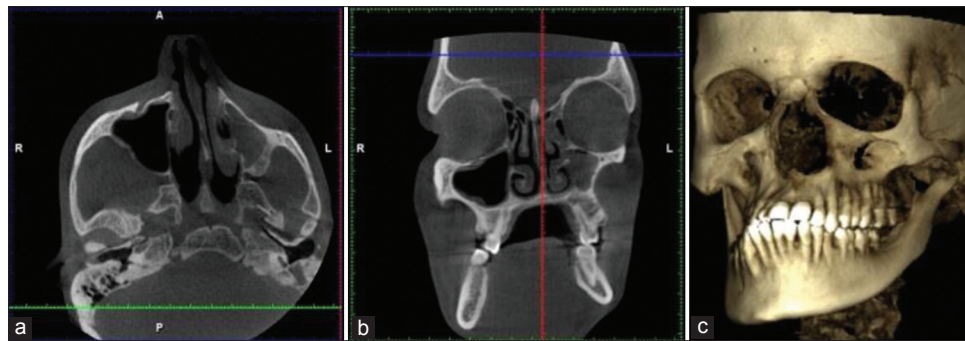


**Figure 9: Posterior-anterior view showing osseous asymmetry**



**Figure 10: Transpharyngeal view showing absence of condylar head and neck with reduced ramus width on left side causing elongation of ramus**





**Figure 11: Cone beam computed tomography (a) axial image (b) coronal image (c) three-dimensional image showing hypoplastic maxilla and mandible on left side**

modification of Pruzansky's grading system, in a Kaban Type IIA, the temporomandibular joint, ramus and glenoid fossa are hypoplastic, malformed and malpositioned, but the deformed joint is adequately positioned for symmetric opening of the mandible. Reported case can be classified into this category based on these features.

The clinical picture of HFM varies from a little asymmetry in the face, to severe under-development of one facial half, with orbital implications, a partially formed ear or even a total absence of the ear. This extreme variability of expression for HFM is especially recognized by facial asymmetry. This is due in part to the absence, hypoplasia, and/or displacement of the pinna, but the degree of involvement is markedly variable. Malformation of the external ear may vary from a complete aplasia to a crumpled, distorted pinna that is displaced anteriorly and inferiorly.<sup>1</sup> Maxillary, temporal, and malar bones on the involved side are somewhat reduced in size and flattened.

Strömmland *et al.* 2007<sup>11</sup> performed prospective multidisciplinary study on Swedish patients with the oculo-auriculo-vertebral spectrum. Most frequent systemic malformations included, ear abnormalities (100%), ocular malformations (72%) was noted. In his study, only 28% patients found to be associated with both visual and hearing impairment which were present in this patient. Consistent findings like vertebral deformities (67%), cerebral anomalies (50%), and rare features such as congenital heart defects (33%), mental retardation (39%), and severe autistic symptoms (11%) were not reported in the present case.

The degree of underdevelopment of the bone is directly related to the hypoplasia of the muscle to which they are attached.<sup>12</sup> In most cases, there is an underdeveloped condyle, but aplasia of the mandibular ramus and/or condyle with the absence of one-glenoid fossa may also occur. In these cases, the maxilla is hypoplastic on the affected side<sup>13</sup> in present patient hypoplasia of malar bone, maxilla and ramus on the left side were present.

Terzis and Anesti<sup>14</sup> in a review on developmental facial paralysis reported that facial palsy was present in 22-50% of patients with HFM. Dysmorphogenesis of the temporal bone and its effects on the facial nerve are most likely implicated in the cause of facial weakness. Congenital malformations associated facial palsy has a poor prognosis for recovery. Facial palsy affects the eye, causing lagophthalmos, ectropion, decreased tear production and corneal damage. In this case, lagophthalmos resulted in exposure keratosis of left eye. In these cases, great attention should be paid to prevent corneal drying, especially at night. Tarsorrhaphy is suggested for severe forms of lagophthalmos. Unilateral colobomas of the superior lid is a common finding. Coloboma of the iris of left eye was noted in the present case.

Mild-to-severe ear findings have been reported, including flattened helical rim off pinna, preauricular skin tags, microtia, external auditory canal atresia, ossicular malformations, and anotia.<sup>8,10-12</sup> Conduction deafness due to middle ear abnormalities and/or absence or deficiency of the external auditory meatus has been noted. No such ear tags were found in this patient, but profound SNHL was noted on audiometric examination.

The incidence of delayed tooth development with HFM is proportional to the extent of mandibular deformity<sup>15</sup> intraoral deformities include delay of tooth development on the affected side hyperplastic or aplastic teeth and enamel. Chalky opacifications of enamel are occasionally found on the maxillary central and lateral incisors of the underdeveloped side as a marker of development for HFM. No such intraoral findings were seen in the present case.

Skeletal alterations are other common anomalies of HFM; HFM patients exhibits occipitalization of the atlas, cuneiform vertebra, cervical complete or partial synostosis of 2 or more vertebrae, supernumerary vertebrae, spinal bifida, and anomalous ribs.<sup>16</sup> No such findings were noted in the present case.



## Treatment

It must be recognized that there is no prescribed treatment program for the child with craniofacial microsomia. The factors such as growth and development and prior therapy, must be considered before recommending an individualized treatment program. Surgical correction of the unilateral deformity is challenging. In patients older than 15 years of age, surgery is often indicated in the period of skeletal maturity. Consequently, all treatment plans must be customized according to the needs and age of the individual patient. When craniofacial growth and development are almost complete, limited autogenous bone grafting of deficient portions of the craniofacial skeleton could be considered.

## CONCLUSION

The purpose of this article is to add one new interesting case with typical clinical and radiological features of HFM and to point out that whenever such case is encountered, the dental radiologist should critically evaluate the temporal bone as inner ear anomalies though rare, can occur in association with HFM.

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# A Fall Can Cause Horrific Complication as a Vault Rupture

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## Abstract

Vault rupture after hysterectomy is a rather rare complication. It can occur after fall specially if there is any penetrating injury. It has also been reported after acts which increase intra-abdominal pressure such as sneezing, coughing, straining during defecation or lifting heavy weight. Most cases of vault rupture have been reported after sexual intercourse. Risk factors include increased age, vaginal surgeries, exposure to radiation. Recent studies have shown increasing incidence of vault rupture after laparoscopic hysterectomy than other methods of hysterectomy. It needs immediate management specially when associated with profuse hemorrhage or prolapsed intestines. Here we are reporting a case of vault rupture occurring after fall on buttocks.

**Keywords:** Dehiscence, Post hysterectomy complications, Vault rupture

## INTRODUCTION

Post hysterectomy patients very rarely<sup>1</sup> (0.1-4.1%) present with complications of vault rupture, specially as a late complication. It is mostly associated with symptoms like dragging pain, vaginal fullness, discharge per vaginum or bleeding per vaginum. It was earlier thought to be more commonly associated with vaginal hysterectomies<sup>2</sup> but recent studies show higher association with abdominal route of hysterectomy especially minimal access surgeries. Vault rupture is mostly seen associated with sexual intercourse<sup>1</sup> (8-48%). But vault rupture due to fall with no penetrating injury is extremely rare. The rare nature of this case prompted us to report this case.

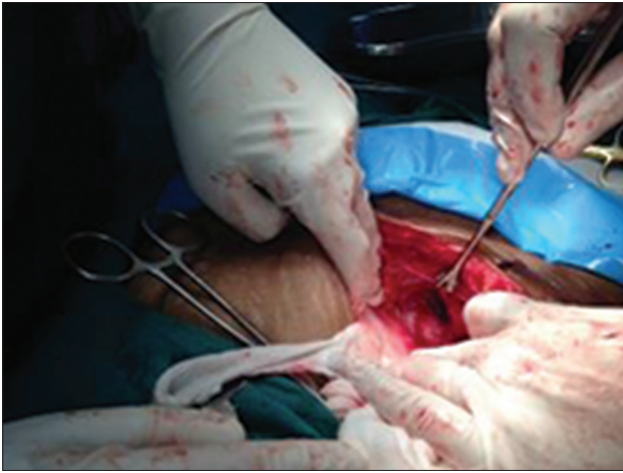
## CASE REPORT

Patient X, 40-year-old female presented to the gynae casualty with history of the fall on buttocks in the bathroom, following which she had developed profuse bleeding per vaginum. There was no history of the fall on any object or any penetrating injury. There was no history of recent sexual intercourse. Patient was P4L4, all four vaginal deliveries with last child birth being 12 years back. She had undergone abdominal hysterectomy for simple hyperplasia of endometrium 2 years back. Her

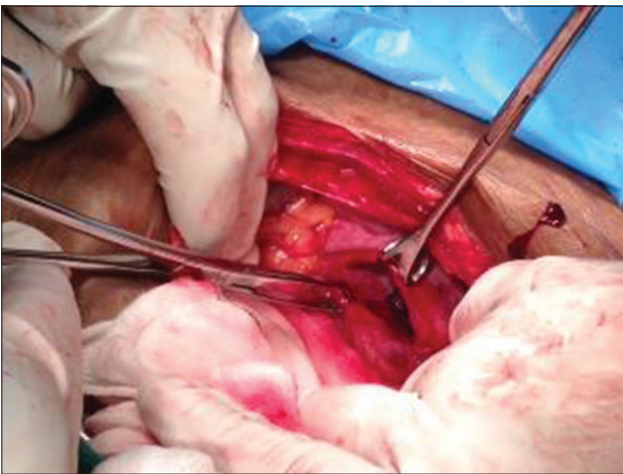
post-operative period then was uneventful. Patient had no other significant medical or surgical history.

On examination, she had marked pallor, tachycardia and low-volume pulse. Her blood pressure was 70/50 mm of Hg. Chest and cardiovascular examination were unremarkable. There was no external sign of injury. Per abdomen examination, there was lower abdomen fullness and tenderness. Local examination showed bleeding per vaginum. Per speculum examination, there was a 4 cm rent on the vault with small bowel seen through it and bleeding from margins of the vault.

Patient was resuscitated with blood and intravenous (IV) fluids and colloids and emergency laparotomy was performed. Minimal amount of hemoperitoneum was present. There was a rent of around 6 cm on the vault, and right angle of vault had a deep laceration which was actively bleeding (Figures 1 and 2). Rest of the abdominal organs were explored by surgeon for any blunt trauma and were found to be normal. Vaginal laceration was repaired, and vaginal packing done which was removed after 24 h. Patient was given 4 units of blood, IV antibiotics and analgesics in post-operative period. Her urinary catheter was removed after 2 days. Patients post-operative period was uneventful and was discharged on post-operative day 5. On follow-up visit, she was all right.



**Figure 1: The intra-operative picture of the open vault seen during laparotomy**



**Figure 2: Closer view of the open vault**

## DISCUSSION

Vaginal cuff dehiscence after hysterectomy is a rare event. It can also occur spontaneously or following trauma or vaginal instrumentation, or any event that increases intra-abdominal pressure.<sup>2</sup> In the cases of vaginal cuff dehiscence reported previously, 8-48% had a history of recent intercourse, and 16-30% reported defecation or valsalva (cough or sneeze) as the precipitating event.<sup>1</sup> However, spontaneous vaginal cuff dehiscence has been reported to represent up to 70% of cases.<sup>3,4</sup> In a study by Hur *et al.*<sup>5</sup> 60% of patients reported with vault dehiscence after history of sexual intercourse. Case report of vault dehiscence after fall on buttocks is very rare. Similar type of case was reported by Pelikan and Engelen.<sup>6</sup> They reported vault rupture in a post hysterectomy patient who presented with pain, bleeding and swelling in the vagina following fall on buttocks. Increased risk of vaginal cuff dehiscence is also associated with increased age, increased number of vaginal surgeries, vaginal atrophy, factors associated

with poor wound healing (including malignancy, chronic steroid use, malnutrition, tissue radiation), increased valsalva (chronic cough), and post-operative vaginal cuff infection or hematoma.<sup>2</sup> Vaginal cuff dehiscence may present as a surgical emergency like in our case, and the approach to therapy for it may be abdominal, vaginal or a combination of the two. Vaginal cuff dehiscence can occur at any time after a pelvic surgical procedure and has been reported as early as 3 days<sup>7</sup> and as late as 30 years post-operatively.<sup>8</sup> When analyzing the risk factors associated with vault rupture it was found that in older reviews of the literature, the majority of cases reported in the literature had occurred after vaginal hysterectomy (63%).<sup>2</sup> In a review done by Hur *et al.*<sup>5</sup> on all hysterectomies performed at single institution over a 6 years period, they found that the incidence of vaginal dehiscence increased from 0% to 0.7% between 2000 and 2006. These increased rates of dehiscence may be related to increased utilization of minimally invasive hysterectomy techniques. Studies have reported rates of 1.1-4.9%<sup>3,5</sup> for cuff dehiscence after total laparoscopic hysterectomy (TLH) and 3% after robotic hysterectomy compared to rates of 0.29% and 0.12% after total vaginal hysterectomy (TVH) and total abdominal hysterectomy (TAH), respectively.<sup>3</sup> In another study done by Hur *et al.*<sup>9</sup> in which they did a cohort study from 2006 to 2009 they concluded that the incidence after TLH was 0.75%, which was the highest among all modes of hysterectomy, laparoscopically assisted vaginal hysterectomy was 0.46%, TAH was 0.38% and TVH was 0.11%. One study showed that patients undergoing TLH have 21 times and 53.2 times the risk of having a vaginal cuff dehiscence compared to patients who had a TVH or TAH, respectively.<sup>5</sup> Koo *et al.*<sup>10</sup> studied 9973 patients of hysterectomy, among which 37 (0.37%) cases of vaginal cuff dehiscence were identified. The incidence of vaginal cuff dehiscence was significantly higher after abdominal hysterectomy (0.6%) than after laparoscopic (0.2%) or vaginal (0.4%) hysterectomy. Patients reporting with vaginal cuff dehiscence may report with symptoms like excessive bleeding per vaginum, discharge per vaginum or pain abdomen. Patients with evisceration of bowel present with pressure symptoms or something coming out per vaginum.

## CONCLUSION

Vaginal cuff dehiscence occurring after fall on buttocks is a rare phenomenon and is mostly associated with an increase in intra-abdominal pressure caused due to the fall. The abdomino vaginal route is the preferred method of repair as it helps in ruling out and repairing all injuries that could be associated. No definite evidence has been found for any technique for vault closure for decreasing the incidence

of vault rupture. Only timely intervention can reduce the morbidity and mortality and long-term complications.

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# Gorlin-Goltz Syndrome: Report of Two Cases

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## Abstract

Gorlin-Goltz syndrome is a genetic disorder transmitted by an autosomal dominant gene with variable expressivity. It is characterized by disorders affecting multiple systems including skeletal, cutaneous, ophthalmic, reproductive, and nervous systems. Multiple odontogenic keratocysts (OKCs) are a principle feature of nevoid basal cell carcinoma syndrome (NBCCS; Gorlin syndrome). It is important to recognize when a patient present with multiple OKCs since the possibility of developing NBCC later in life cannot be excluded. This article describes two cases presented with multiple odontogenic cysts of jaws which can be considered partial expression of NBCCS.

**Keywords:** Gorlin-Goltz syndrome, Multiple odontogenic keratocysts, Nevoid basal cell carcinoma syndrome

## INTRODUCTION

Odontogenic keratocysts (OKCs) constitute 3-11% of the odontogenic cysts of the jaws.<sup>1</sup> First described by Philipsen in 1956, they are considered developmental cysts of epithelial origin.<sup>1</sup> Multiple OKCs may occur in association with jaw cyst basal cell nevus syndrome or Gorlin-Goltz syndrome. In 1960 Gorlin and Goltz studied the main features of this disorder, hence the name.<sup>2</sup> It is characterized by disorders affecting multiple systems including skeletal, cutaneous, ophthalmic, reproductive and nervous systems.<sup>2</sup> Nevertheless complete expression of this syndrome is rare. Most patients present with the chief complaint of jaw swelling from which the diagnosis is often made.<sup>3</sup>

Occurrence of nevoid basal cell carcinoma syndrome (NBCCS) has been observed even in ancient Egyptian skeletons of the dynastic period.<sup>4</sup> The first reported literature dates as early as 1894, wherein Jarisch and White described a patient with this syndrome, highlighting the presence of multiple basocellular carcinomas (BCCs).<sup>4</sup> The estimated prevalence varies from 1 in 57,000 to 1 in 256,000 with a male:female ratio of 1:1.<sup>5</sup> The two case reports with review of literature described below can be considered partial expressions of the syndrome.

## CASE REPORTS

### Case 1

A 15-year-old male patient presented with complaint of swelling and associated pain in relation to right maxillary posterior region of 6 months duration. He gave a history of swelling over hand 1-year back for which excision was done in a local hospital. No detailed reports were available for the same. Extra-oral examination revealed mild frontal bossing, wide and depressed nasal bridge and hypertelorism (Figure 1). Intra-orally there was a palpable firm tender swelling approximately 2 cm × 2 cm in relation to mucobuccal fold opposite 26, 27 region (Figure 2). Similar non tender swelling was observed in relation to 17 region. 17, 18, 28, 38, 47, and 48 were clinically missing. The alveolar mucosa appeared edematous in these regions.

Panoramic radiograph revealed multiple well defined unilocular pericoronal radiolucencies in relation to impacted 18, 28, 38 and 48. Tooth buds of 28, 48 appear displaced (Figure 3). A well-defined radiolucency was observed in relation to interdental region 42, 43 region with associated teeth displacement (Figure 4).

Computerized tomography scan showed 4 well defined non enhancing radiolucent lesions involving maxilla

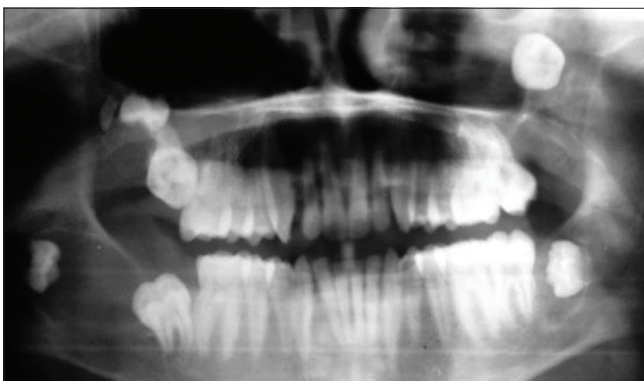
and mandible with associated impacted teeth (Figures 5 and 6). Largest of the lesions in the alveolar process of the left maxilla extending into the left maxillary sinus. It



**Figure 1:** Extraoral photograph showing mild frontal bossing, wide and depressed nasal bridge and hypertelorism



**Figure 2:** Intraoral photograph showing firm tender swelling approximately 2 cm x 2 cm in relation to mucobuccal fold opposite 26, 27 region



**Figure 3:** Panoramic radiograph revealing multiple well defined unilocular pericoronal radiolucencies in relation to impacted 18, 28, 38 and 48. Tooth buds of 28, 48 appear displaced

measured 21 mm x 38 mm causing expansion of left maxillary sinus. Another cyst in the left mandible measured 27 mm x 15 mm with 37 within the lesion. Cystic lesion associated with 47, 48 measured 15 mm x 30 mm. Another cystic lesion in the right maxilla measured 20 mm x 19 mm with 18 projecting into the maxillary sinus

General examination didn't reveal any cutaneous abnormalities. Bifid-rib anomaly was evident with respect to right fifth rib on chest X-ray (Figure 7). Hematologic results were within normal limits.

Patient underwent enucleation of the cysts under general anesthesia in the Department of Maxillofacial Surgery and specimen was send to Department of Oral Pathology.

Histopathological report showed a cystic capsule lined by a corrugated epithelium having uniform thickness showing



**Figure 4:** Intraoral periapical showing well defined radiolucency in relation to interdental region 42, 43 region with associated teeth displacement



**Figure 5:** Computerized tomography scan showed 2 well defined non enhancing radiolucent lesions involving maxilla with associated impacted teeth

proliferation in some areas (Figure 8). The lining parakeratinised stratified squamous epithelium showed palisading of basal cells. The capsule exhibits forming daughter cysts in areas. These features were suggestive of OKC.

## Case 2

A 9-year-old female patient presented with the complaint of painful swelling in relation lower jaw of 2 weeks duration. Extra-oral examination revealed a diffuse swelling in relation to left parasymphysal region of size approximately 5 cm × 4 cm. She had mild frontal bossing, wide and depressed nasal bridge and hypertelorism (Figure 9). Intra-orally there was a fluctuant swelling obliterating lower buccal sulcus opposite 33-36 region approximately 3 cm × 2 cm size (Figure 10). Family history was non-contributory.

Panoramic radiograph shows well defined unilocular radiolucency involving the left parasymphysis with 33 and 34 pushed to the lower border of mandible. There were

multiple large radiolucencies involving bilateral ramus. Associated displacement of 47 and 37 were seen (Figure 11).

Chest radiograph revealed bifid-rib anomaly with respect to right third rib (Figure 12). Cysts were enucleated under general anesthesia and send for histopathologic examination. Histopathological examination results were consistent with that of OKC (Figure 13).

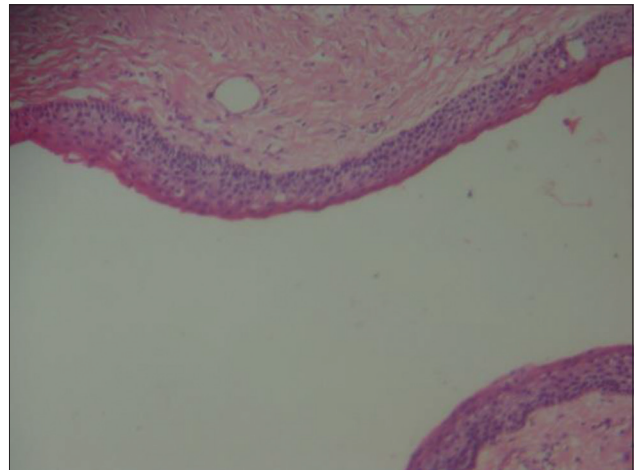
## DISCUSSION

Multiple OKCs of the jaws can occur in association with NBCCS or Gorlin-Goltz syndrome,<sup>6</sup> orofacial digital syndrome,<sup>7</sup> Noonan syndrome,<sup>8</sup> Ehler-Danlos syndrome or Simpson-Golabi-Behmel syndrome.<sup>9</sup>

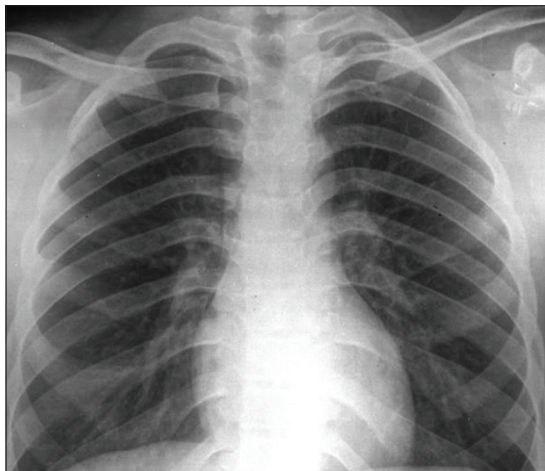
Approximately 4-5% of multiple OKCs are associated with NBCCS.<sup>10</sup> Naevoid basal cell carcinoma syndrome is a rare



**Figure 6:** Computerized tomography scan showed 2 well defined non enhancing radiolucent lesions involving mandible with associated impacted teeth



**Figure 8:** Histopathological report showed a cystic capsule lined by a corrugated epithelium having uniform thickness showing proliferation in some areas



**Figure 7:** Bifid-rib anomaly was evident with respect to right fifth rib on chest X-ray

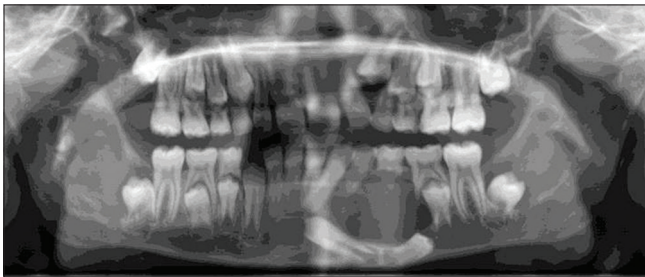


**Figure 9:** She had mild frontal bossing, wide and depressed nasal bridge and hypertelorism





**Figure 10:** Intraorally there was a fluctuant swelling obliterating lower buccal sulcus opposite 33 to 36 region approximately 3 cm x 2cm size



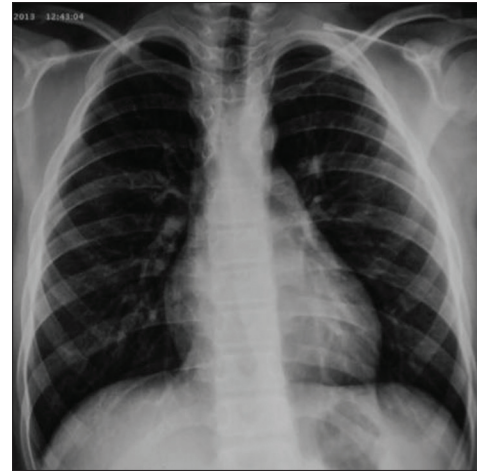
**Figure 11:** There were multiple large radiolucencies involving bilateral ramus. Associated displacement of 47 and 37 were seen

pleiotropic autosomal dominant condition often presenting at an early age in life.<sup>10,11</sup> It is caused by mutations in the PTCH1 gene and exhibit complete penetrance and variable expressivity.<sup>11</sup> Diagnosis of NBCCS is often made from the criteria given by Evans *et al.* (Table 1).<sup>12</sup> 2 major or 1 major and 2 minor criteria should be satisfied for positive diagnosis.

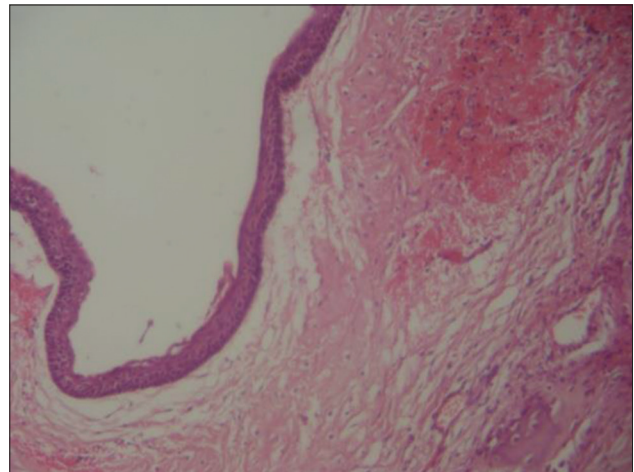
Less than 10% of the patients with multiple OKC have other manifestations of this syndrome.<sup>10</sup> Multiple OKC may be the only feature in some cases and may appear early in life, while other features remain hidden.<sup>3</sup>

Both the patients in our study were below 15 years of age. Both presented with jaw swelling. Clinical examination revealed mild frontal bossing, hypertelorism, wide nasal bridge in both the cases. Head circumference was more in the second case. Cutaneous abnormalities were not evident.

Radiographically, OKCs present as well defined radiolucent lesions with smooth, usually corticated margins and may be either multilocular or unilocular.<sup>13</sup> It may present with scalloped borders indicative of varying growth pattern.<sup>14</sup> There is involvement of an unerupted tooth with no apparent root resorption in most cases.<sup>14</sup> In both the cases



**Figure 12:** Chest radiograph revealed bifid-rib anomaly with respect to right third rib



**Figure 13:** Histopathological examination results were consistent with that of odontogenic keratocyst

described above there were unerupted teeth associated with well-defined unilocular radiolucencies.

Histopathologic features of OKC are characteristic. The cyst wall is rather thin, with a parakeratinized or orthokeratinized surface that is typically corrugated. There is remarkable uniformity in the thickness of the epithelium.<sup>14,15</sup>

Studies have shown that parakeratinization, intramural epithelial remnants and satellite cysts are more frequent among OKCs associated with NBCCS than in solitary keratocysts.<sup>16</sup> In both the cases the lining of the OKCs revealed the presence of parakeratinization and developing microcysts in the connective tissue wall indicating NBCCS association. Table 2 describes the characteristics of NBCCS associated and non-associated OKCs.

The gene whose mutations cause NBCCS has been mapped to the long arm of chromosome 9q22.3.<sup>11</sup> Studies have



**Table 1: 2 major or 1 major and 2 minor criteria should be satisfied for positive diagnosis**

Major criteria
More than 2 BCCs, 1 BCC before 30 years of age; or more than 10 basal cell nevi
Any odontogenic keratocyst (proven on histology) or polyostotic bone cyst
3 or more palmar or plantar pits
Ectopic calcification; lamellar or early (<20 years of age) falx calcification
Family history of nevoid basal cell carcinoma syndrome
Minor criteria
Congenital skeletal anomaly (e.g., bifid rib, fused, splayed or missing rib, wedged or fused vertebrae)
Occipital-frontal circumference higher than the 97 <sup>th</sup> percentile, with frontal bossing
Cardiac or ovarian fibroma
Medulloblastoma
Lymphomesenteric cysts
Congenital malformations, such as cleft lip or palate, polydactylism or eye anomaly (cataract, coloboma, microphthalmos)

BCCs: Basal cell carcinomas

**Table 2: Comparison of clinical and histological features of NBCCS associated and solitary OKCs**

NBCCS associated OKC	Solitary OKC
Clinical characteristics	
Occur at an early age	Occur at middle or older age
Multiple cysts	Isolated cysts
Occur in both jaws with equal frequency	Occurs more often in the lower jaw
Higher recurrence rate (82%)	Lower recurrence rate (61%)
Histological characteristics	
Smaller epithelial height	Greater epithelial height
Fewer total and basal nuclei	More total and basal nuclei
More frequent occurrence of odontogenic islands and daughter cysts	Less frequent occurrence of odontogenic islands

NBCCS: Nevoid basal cell carcinoma syndrome, OKCs: Odontogenic keratocysts

demonstrated loss of heterozygosity of this region of 9q22.3 in DNA from familial and sporadic BCCs and OKCs.<sup>11</sup> The underlying genetic defect in NBCCS has been proposed to be a mutation in a tumor suppressor gene, as evidenced by the relatively early occurrence of multiple BCCs and multiple recurrent OKCs.<sup>11</sup> NBCCS patients have been found to carry 9 variants of mutations.<sup>11</sup> the negative family history in both of our patients can be attributed to this variation.

Hence both the cases can be considered partial expressions of NBCCS (Table 3).

OKCs associated with Gorlin-Goltz syndrome are more aggressive and these cysts have higher recurrence rate.<sup>17</sup> The higher recurrence rates are attributed to the presence of satellite cysts or remnants of cyst lining left behind following surgery.<sup>18</sup>

**Table 3: Comparison of features of both cases**

Features	Case 1	Case 2
Ophthalmologic	Wide nasal bridge hypertelorism	Wide nasal bridge hypertelorism
Cutaneous	Nil	Nil
Skeletal	Frontal bossing bifid 5 <sup>th</sup> rib	Frontal bossing bifid 3 <sup>rd</sup> rib
Dental	Multiple OKCs of jaws	Multiple OKCs of jaws

OKCs: Odontogenic keratocysts

The ideal treatment for the OKCs would be enucleation or curettage followed by treatment of the cavity with an agent that would kill the epithelial remnants or satellite cysts.<sup>18</sup> In addition, the osseous framework should be left intact to allow for osteoconduction.<sup>18</sup> The use of Carnoy's solution or liquid nitrogen cryosurgery following enucleation helps prevent recurrences.<sup>18,19</sup> The unique ability of liquid nitrogen to devitalize bone *in situ* while leaving the inorganic framework untouched is used to kill epithelial remnants and dental lamina within the osseous margin.<sup>19</sup>

## CONCLUSION

The possibility of these young patients developing NBCCS later in life cannot be excluded.<sup>20</sup> Long-term follow-up of these young patients is mandatory. A dental surgeon can play a major role in the early diagnosis and appropriate referral in case of OKC associated NBCCS.

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# Kimura's Disease: A Rare Cause of Local Lymphadenopathy

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## Abstract

Kimura's disease is a rare chronic inflammatory disorder of unknown etiology, primarily seen in young Asian males, especially in Chinese and Japanese, though rare in Indians. The disease is characterized by a triad of painless cervical adenopathy or subcutaneous masses in the head or neck region, blood and tissue eosinophilia, and markedly elevated serum immunoglobulin E levels. Although it may mimic a neoplastic process, the disease is slowly progressive benign condition leading to difficulty in making the correct diagnosis. Early diagnosis of Kimura's disease may spare the patient from potentially harmful and unnecessary invasive diagnostic procedures. We report a case of Kimura's disease in a young Indian male presenting with bilateral postauricular swellings with review of the literature.

**Keywords:** Eosinophilic lymphogranuloma, Glomerulonephritis, Immunoglobulin E, Kimura, Subcutaneous nodules

## INTRODUCTION

The first known report of Kimura disease was from China in 1937, when Kimm and Szeto who termed it as the "eosinophilic hyperplastic lymphogranuloma."<sup>1</sup> It received its current name in 1948, when Kimura *et al.* noted a change in the surrounding blood vessels and referred to it as unusual granulation combined with hyperplastic changes in lymphoid tissue.<sup>2</sup> Although it may mimic a neoplastic process, it is a rare benign idiopathic chronic inflammatory disorder. It is characterized by a triad of painless unilateral cervical adenopathy or painless subcutaneous masses in the head or neck region, blood and tissue eosinophilia, and markedly elevated serum immunoglobulin E (IgE) levels.

The disease is endemic to Asians (especially in China and Japan),<sup>2-4</sup> but rare in India, with about 200 reported cases worldwide since its histopathological diagnosis. Non-Asian cases also have same histopathological features. There is marked male predominance with M:F ratio 3.5-7:1. Peak age incidence is in third decade. Treatment options such as complete surgical excision, steroids, radiotherapy, etc. are tried with variable responses. Recurrence is common with all the modalities of treatment.

## CASE REPORT

An 18-year-old Indian male presented with the complaints of swelling behind both ears, which was gradually increasing in size since 2 years. Except the local pruritus, he had no additional complaint related to the swellings or any constitutional symptoms. Physical examination revealed two distinct palpable masses at the both postauricular areas, which were non-fluctuant, firm, soft, rubbery, non-tender, freely mobile and of about 4 cm × 3 cm size (right > left) (Figure 1). The rest of the general physical as well as systemic examinations were normal.

Peripheral blood smear showed 13% eosinophils with absolute eosinophil count of 1140/mm.<sup>3</sup> Computed tomography (CT) scan temporal bone were performed to assess the extent and any intracranial extension of the lesion. Chest radiograph was within normal limits. A tuberculosis skin test (purified protein derivative skin test) was negative.

A simultaneous excisional biopsy and histopathological examination of the both postauricular lesions was made. Histopathology showed eosinophilic infiltration and vascular proliferation (Figures 2 and 3) and a prominent

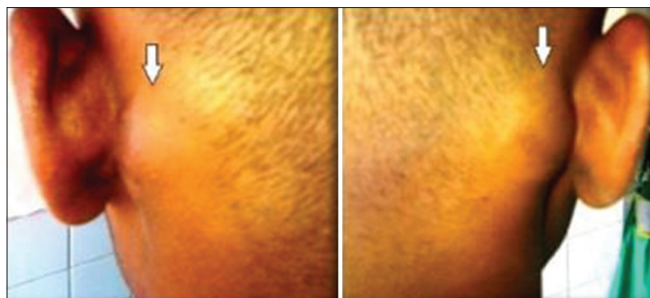
vascularity within the extranodal soft tissues associated with lymphoid hyperplasia and sheets of eosinophils. The associated lymph nodes showed florid follicular hyperplasia, with focal eosinophilic microabscess formation within the paracortex and interfollicular region. Several germinal centers showed disruption by large aggregates and sheets of eosinophils. All these features suggested the diagnosis of Kimura's lymphadenopathy.

Accordingly, serum IgE levels were estimated which showed marked rise >3000.00 KIU/ml (normal range:

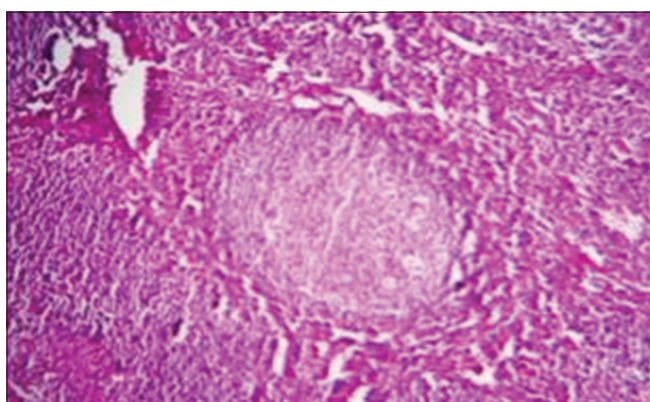
0-150 KIU/ml), thus further supported the diagnosis. Assessment of renal function was normal, and there was no evidence of proteinuria. Based on the clinical, histopathological and specific laboratory findings, the final diagnosis of Kimura's disease was made.

The treatment with oral prednisolone was started at a dose of 40 mg/day for the initial period of 1 week, and subsequently tapered every week by 10 mg/day over period of the next 4 weeks.

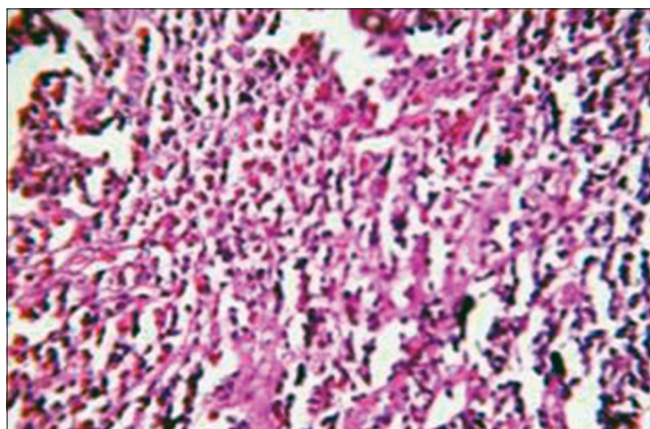
After 1 week of treatment, eosinophilia was decreased significantly and became well within normal limits in 2 weeks. IgE levels fell to 140 KIU/ml gradually. There was no local recurrence at the 24 months follow-up.



**Figure 1: Clinical photographs of postaural swellings**



**Figure 2: x100 microphotograph of the excision biopsy specimen showing a lymph node with florid germinal centre paracortical eosinophilic infiltrates, eosinophilic microabscess**



**Figure 3: x400 microphotograph of the same, showing paracortical eosinophilic infiltrates**

## DISCUSSION

The disease typically presents with insidious onset of painless subcutaneous masses or adenopathy in the head and neck region<sup>4</sup> with the occasional pruritus of the overlying skin.<sup>5,6</sup> The disease usually involves subcutaneous tissues, lymph nodes (periauricular, axillary, and inguinal), parotid and submandibular salivary glands, and rarely, oral mucosa.<sup>4,7</sup>

The clinical course of Kimura's disease is generally benign and self-limited. Most patients have a prolonged course with slow enlargement of the masses. Occasional spontaneous resolution is known. These lesions do not have any malignant potential. Kimura's disease may be complicated by renal involvement. In cases of renal involvement, nephrotic syndrome is the commonest presentation,<sup>8</sup> proteinuria may occur in 12-16% of cases.<sup>8</sup> A wide spectrum of histologic lesions has been described<sup>9</sup> wherein extra membranous glomerulonephritis is found in up to 60% of patients.

In our case, there is normal renal function and no evidence of proteinuria.

The exact cause and pathogenesis of Kimura's disease is unclear, although it might be a self-limited allergic or autoimmune response triggered by an unknown persistent antigenic stimulus. Peripheral eosinophilia and the presence of eosinophils in the inflammatory infiltrate suggest that Kimura's Disease may be a hypersensitivity reaction. None of these theories has been substantiated till date.

Immunohistochemical studies have shown marked proliferation of human leukocyte antigen-DR CD4 cells<sup>10</sup> which release eosinophil-trophic cytokines (interleukin-4 [IL-4], IL-5,<sup>11</sup> and IL-13)<sup>6</sup> which in turn may precipitate the



high serum IgE and eosinophilia.<sup>12</sup> This suggests that these cytokines may have a role in the pathogenesis.

Immunoperoxidase studies show IgE reticular network in germinal centers and IgE coated non-degranulated mast cells.<sup>4</sup>

The pathology of Kimura's disease is characterized by prominent germinal centers in involved lymph nodes containing cellular, vascular, and fibrous components.<sup>13,8</sup> The cellular component consists of dense eosinophilic infiltrates in a background of abundant lymphocytes and plasma cells, eosinophilic microabscesses with central necrosis. The histopathological features of Kimura's disease are typical and allow its differentiation from other diseases that present similarly.

As the clinicians and pathologists may be unfamiliar with clinical and pathological presentation of this rare condition, the diagnosis of Kimura's disease can be difficult one. Therefore, the laboratory tests become essential in making correct diagnosis. The differential leukocytic count (DLC) almost always reveals peripheral eosinophilia (98%) and elevated serum IgE levels are seen in patients with Kimura disease.<sup>2</sup> The number of eosinophils on DLC can be closely correlated to the sizes of the neck masses.

Imaging studies such as CT and magnetic resonance imaging (MRI) are useful only in delineating the extent of the disease. Findings of intense contrast enhancement on CT scan and high T1- and T2-weighted signal intensities on MRI in parotid glands and lymph nodes have been described.<sup>14</sup>

The diagnosis is made by histopathological examination of excisional biopsy of the lesion.

Patients with Kimura's disease are often extensively evaluated for other serious disorders, including neoplasia (e.g., acute non-lymphocytic leukemia and Hodgkin disease and follicular lymphoma). Kimura's disease can mimic other disorders such as Mikulicz's disease, eosinophilic granuloma, malignancies and salivary gland tumors. Other differential diagnoses include angiolymphoid hyperplasia with eosinophilia,<sup>15</sup> cylindroma, dermatofibrosarcoma protuberans, Kaposi sarcoma, and pyogenic granuloma (lobular capillary hemangioma).

There is no consensus on the management of Kimura's disease. Various treatment modalities have been tried with variable success.

At initial presentation, surgical biopsy is the most frequent diagnostic procedure performed. For the localized

disease, complete surgical excision of the lesion(s) may be curative. Recurrences have been reported, particularly after incomplete removal. Localized initial regrowth can often be managed with repeat surgical excision.

The goals of pharmacotherapy of Kimura's disease are to reduce morbidity, prevent complications and observation for the recurrence. Observation is acceptable if the Kimura's disease lesions are neither symptomatic nor disfiguring.

The pharmacotherapy of Kimura's disease has mainly involved the use of oral corticosteroids for an adequate period and tapered off gradually. The abrupt termination of steroid therapy often results in a relapse. Systemic steroids may be indicated infrequent relapses or cases complicated by nephrotic syndrome. The chronic steroid therapy poses its additional risks. Intralesional steroids (eg., triamcinolone acetonide) can shrink the nodules, but seldom result in the cure.

Radiotherapy has occasionally been used to treat recurrent, persistent or refractory cases to surgical and medical therapy, recalcitrant and large lesions, young patients or when surgery is not feasible. However, regrowth of the lesion is common after discontinuing such treatment.

Cyclosporine,<sup>10</sup> oral pentoxifylline, all trans-retinoic acid with prednisone,<sup>10</sup> imatinib have been tried in the treatment for Kimura's disease with variable responses. Cetrizine is suitable for the treatment of the pruritus associated with these lesions.

It is also thought that the inhibition of eosinophils may be the key in treatment of Kimura's disease, rather than other cells with regards to the lesions of the skin.

The choice of treatment modalities should be individual. Recurrence is common with all the modalities of treatment.

## CONCLUSION

The present case reiterates that Kimura's disease may cause chronic neck masses in young male patients and highlights the need for increased awareness of this clinical entity in clinicians and pathologists to avoid unnecessary and potentially invasive investigations, such as bone marrow aspiration/biopsy and radiological imaging. A suspicion of this condition may be maintained, especially in the presence of slowly progressive swellings or any lymphadenopathy with concomitant eosinophilia or high-IgE levels. All such cases must be looked for and investigated for correct diagnosis and treatment.

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# A Rare Case of Domperidone Induced Oculogyric Crisis in Young Female

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## Abstract

Domperidone being a commonly used drug causing oculogyric crisis (OGC) is a rare entity. OGC is type of the dystonic reaction due to certain drugs. It is the most common of the ocular dystonic reactions (which include blepharospasm, periorbital twitches, and protracted staring episodes). A 32-year-old female came to ophthalmology outpatient clinic with the complaints of inability to move both eyes since afternoon associated with neck rigidity, anxiety and difficulty in breathing. She had a history of acute gastroenteritis for past 1 day and was treated with tablet ciprofloxacin (500 mg twice daily) tablet domperidone (10 mg twice daily) and tablet pantoprazole (40 mg twice daily) on the same day morning and developed the above eye problems in 3 h. All routine investigations and imaging were normal and in doubt of acute dystonic reaction was treated with intravenous diphenhydramine 25 mg BD and she recovered in 2 h we came to the diagnosis of OGC due to domperidone.

**Keywords:** Domperidone, Dystonia, Oculogyric crisis

## INTRODUCTION

Oculogyric crisis (OGC) is an acute dystonic reaction of the ocular muscles characterized by bilateral dystonic elevation of visual gaze lasting from seconds to hours. This reaction is most commonly explained as an adverse reaction to drugs such as anti-emetics, anti-psychotics, anti-depressants, anti-epileptics, and anti-malarials.<sup>1</sup> It is important to be able to recognize this ocular side-effect because, without a thorough patient history, symptoms can be confused with other diseases such as versive seizures, paroxysmal tonic upward gaze, and encephalopathy. OGC makes up 6%.<sup>2</sup> In anti-emetics metachlorpromide induced OGC is common, but domperidone induced OGC is a rare entity, and there are no reports in literature search.

## CASE REPORT

A 32-year-old female came to ophthalmology outpatient clinic with complaints of inability to move both eyes since afternoon associated with neck rigidity, anxiety and difficulty in breathing (Figure 1). She was not having diplopia, fever and seizures and was not a known diabetic or hypertensive. She had acute gastroenteritis

for past 1 day and was treated with tablet ciprofloxacin (500 mg twice daily) tablet domperidone (10 mg twice daily) and tablet pantoprazole (40 mg twice daily) on the same day morning and developed the above eye problems in 3 h. On examination, she was conscious, oriented, agitated and had difficulty in breathing. Vitals were normal. General examination showed that both eyes were hypertrophic, and all the extraocular movements were restricted. Anterior segment examination was normal. Pupils were reacting to both direct and indirect light reflex and fundus was normal. Neck rigidity was present. Motor and sensory system was normal. Routine blood investigations and Serum electrolytes were normal. Computed tomography brain was taken and was found to be normal. Patient was admitted in intensive care unit for observation because of the difficulty in breathing and doubt of acute dystonic reaction was treated with intravenous (IV) diphenhydramine 25 mg BD and she recovered in 2 h (Figures 2-4).

## DISCUSSION

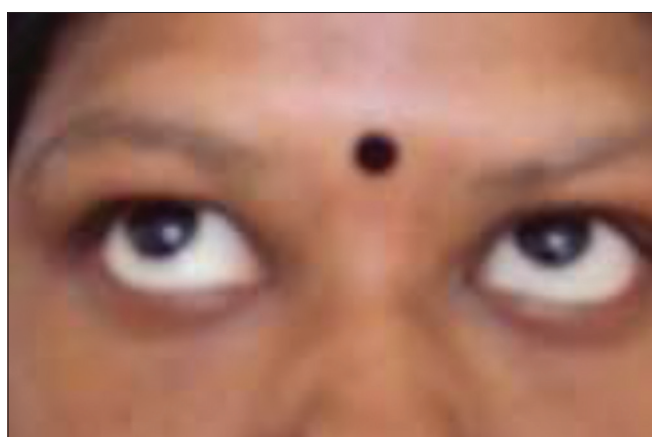
Dystonic reactions are reversibly extrapyramidal effects that may occur after administration of certain drugs,



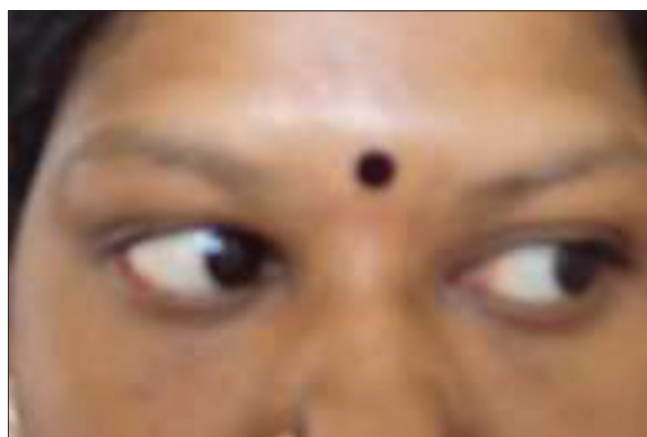
**Figure 1: Patients eyes are hypertrophic on primary gaze**



**Figure 3: After treatment right eye abduction and left eye adduction present**



**Figure 2: All extra-ocular movements restricted**



**Figure 4: After treatment right eye adduction and left eye abduction present**

and they may begin immediately or be delayed.<sup>3</sup> Features of dystonic reactions are intermittent spasmodic or sustained involuntary contractions of the face muscles, pelvis, trunk, extremities, neck or sometimes and even the larynx.<sup>4</sup> Dystonic reactions even though are not life threatening but it causes stress to the patient and the family. Mechanism of dystonic reactions in many drugs is by nigrostriatal dopamine D2 receptor blockade, which in turn causes an excess of striatal cholinergic output. High-potency D2 receptor antagonists mostly will produce an acute dystonic reaction.<sup>5</sup> As there is diminished numbers of D2 receptors in old age there is less risk of dystonia in elderly age.<sup>6</sup> Dystonia is more common in younger females, but the reason is unclear. Dystonic reactions usually occur shortly after initiation of drug; 50% occur within 48 h and 90% usually occur within 5 days of treatment.<sup>7</sup> Acute dystonia can be misdiagnosed and confused with encephalitis, complex partial seizures, tetanus, strychnine poisoning and hypocalcemic tetany so careful history eliciting is important.<sup>8</sup> People with family history of dystonia, recent use of cocaine or alcohol,

treatment with a potent dopamine D2 receptor antagonist are at more risk.<sup>9</sup>

Characteristic of OGC is sustained upward elevation of visual gaze of both eyes with neck hyperextension. Causes of OGC include usage of medications like neuroleptics, metoclopramide carbamazepine, lithium, levodopa, amantadine, chloroquine. Brain stem lesion and head trauma leading to OGC have also been reported.<sup>10</sup> Clinical features of OGC include Involuntary, sustained deviation of the eyes, extension of the neck, restlessness, agitation, behavioral disturbances, transient psychotic episodes visual hallucination and auditory hallucination is also seen in some people.<sup>11</sup>

Treatment in the acute phase involves reassurance and treatment with cogent in (IV or myocardial infarction) and/or benadryl (diphenhydramine) and/or diazepam or lorazepam. Maintenance therapy with oral forms of the above medications or amantadine are indicated in more



chronic recurrent cases.<sup>12</sup> On re-exposure to the drug chances of symptoms occurring again are high.

## CONCLUSION

This case is presented because the incidence of domperidone causing OGC is rare, and domperidone is a common drug which we are using in day-to-day practice. As young doctors, we should be careful before prescribing any drug and ask about drug allergy and take a detailed history asking what medications the patients are on without a thorough history, symptoms can be confused with other diseases, such as partial epileptic seizure with versive movements and eye movement tics. It is necessary for ophthalmologists and general physician to be aware of these side effects and diagnose this early and avoid the trouble for the patient of going through detailed neurological examinations and investigations.

## ACKNOWLEDGEMENT

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# Secondary Esotropia with Bilateral Pseudophakia and its Surgical Management: A Case Report

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## ABSTRACT

Sensory strabismus is frequently associated secondary to congenital cataracts, either unilateral or bilateral. Surgical correction of sensory strabismus is indicated to improve binocular vision and for aesthetic reasons. In the present study, a patient with sensory esotropia secondary to congenital cataract, operated previously for cataract elsewhere; presented with gross diminution of vision in the left eye due to dislocated intraocular lens into the anterior chamber. The patient was treated surgically first with membranectomy and pupilloplasty in the affected eye, followed by consecutive strabismus correction surgery to obtain satisfactory results.

**Keywords:** Congenital cataract, Membranectomy, Myomectomy, Pupilloplasty, Sensory strabismus, Tenotomy

## INTRODUCTION

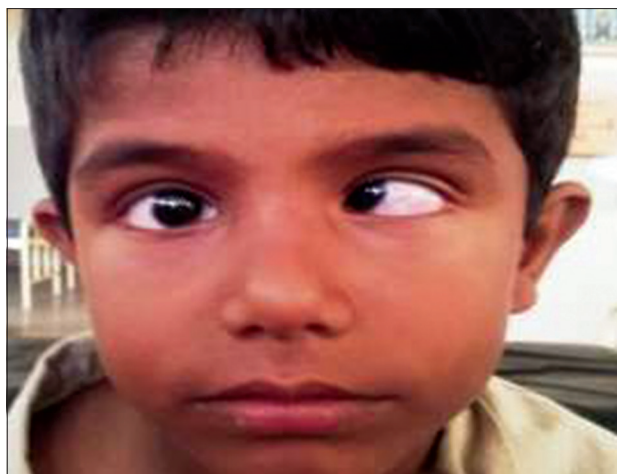
Sensory strabismus is a pathology frequently associated with congenital cataracts, either unilateral or bilateral. According to some authors, the frequency of strabismus prior to cataract surgery is 40%, increasing to 71% after extraction. Esotropia is associated to congenital cataracts, in 83% cases, and exotropia represents a higher incidence in acquired cataracts, with 69% cases.<sup>1</sup> More frequent strabismus has also been observed in unilateral cataracts than in bilateral ones. Implantation of an intraocular lens (IOL) reduces the occurrence of sensory strabismus. Surgical correction of sensory strabismus is indicated to improve binocular vision and for aesthetic reasons. The most appropriate time to perform surgery for strabismus secondary to congenital cataracts is a controversial topic; whereas some authors propose delaying the operation until the angle of deviation is stabilized, and visual rehabilitation is completed, others prefer early surgery to reduce the time of treatment with occlusions.<sup>2</sup>

## CASE REPORT

The case we present here is about a 6-year-old boy who presented with inward turning and gross diminution of

vision in the left eye since 1 year. He was operated 1 year back elsewhere for bilateral congenital cataract. His visual acuity was 6/60 in the right eye and left eye visual acuity was counting finger 1 m, not improving with pinhole. On detailed examination, it revealed posterior chamber IOL (PCIOL) dislocated into the anterior chamber (AC), with cortex in AC in the left eye. The direct cover test revealed marked esotropia with Hirschberg test showing an angle of 45° inward deviation. Extraocular movements showed restriction of the lateral rectus muscle, along with inferior oblique overaction in the left eye. The child also presented with secondary sensory nystagmus. Fundoscopic examination and ultrasound biomicroscopy of the posterior segment revealed no significant abnormality.

The patient was taken up for surgical correction under general anesthesia in two sittings. The displaced PCIOL was corrected with membranectomy and pupilloplasty in the affected eye, followed by AC wash to remove the retained cortex. Three weeks later it was followed by a consecutive strabismus correction surgery of the affected eye again under general anesthesia. Forced duction test pre-operatively showed restriction in abduction (Figure 1). On exposure, the conjunctiva and Tenon's capsule on the medial side of the left eye appeared thickened and fibrosed. The fleshy and thickened tendon of the medial



**Figure 1: Pre-operative**

rectus muscle showed an anomaly of insertion, being only 3 mm away from the limbus. A medial rectus tenotomy and tenectomy was performed along with a myotectomy of the inferior oblique muscle to achieve correction.

Post-operatively, the squinting eye showed marked improvement in alignment and visual improvement of counting finger 4 m (Figure 2).

## DISCUSSION

The association of congenital cataracts with sensory strabismus is presented very frequently with a prevalence of 72.4%.<sup>3,4</sup> Thus, it is important to identify these patients and subject to surgical correction in early life. The outcome of surgery depends on the timing of surgery. Cataract surgery should be performed when patients are younger than 17 weeks to ensure minimal or no visual deprivation. Most ophthalmologists opt for surgery much earlier, ideally when patients are younger than 2 months, to prevent the irreversible amblyopia and sensory nystagmus in the case of bilateral congenital cataracts.<sup>5,6</sup> The delay in surgery is because of glaucoma. Since glaucoma occurs in 10% of congenital cataract surgery, many surgeons delay the cataract surgery. Consecutively, the best time to treat strabismus may be early, as soon as it is diagnosed according



**Figure 2: Post-operative**

to the preference of some authors, or later, after completing visual rehabilitation.<sup>7,8</sup>

## CONCLUSION

Hence, it can be concluded that the aim of treatment is not only to achieve cosmetic improvement, but also improvement in the visual acuity with the restoration of binocular single vision.

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# A Case of Tessier Cleft 1 Presenting as Isolated Coloboma of Nose

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Tessier cleft 1 is an extremely rare congenital anomaly. The severity varies from isolated paramedian cleft involving the dome of the nostril<sup>1</sup> to cleft extending upwards (northbound) through the nasal bone into the cranium

as Tessier cleft 13. Failure of fusion of lateral and medial nasal processes of the frontonasal process may be the cause of the anomaly.<sup>1</sup>

A 22-year-old male attended with a paramedian cleft in the left side of the nose (Figure 1a and b). The cleft extended upwards to end at the lower end of the nasal bone. The nasal septum was slightly deviated to the left side, and there was a bony hump in the dorsum of the nose. There was no obstruction of the nasal passage. Family history was not suggestive. Radiological investigations did not show any bony involvement.

Reconstruction was planned under local anesthesia after routine hematological investigations. A composite mucocutaneous lateral alar flap was rotated to form the alar rim.<sup>2</sup> The defect thus produced was covered with a transposition flap raised from the dorsum of the nose.<sup>2</sup> The donor defect produced by the transposition flap was



**Figure 1: (a and b) Clinical photograph showing the left sided paramedian cleft involving nasal ala**



**Figure 2: (a, b, and c) Post-operative clinical photograph after repair of the nasal cleft**



### Points to Ponder

- 1) Tessier cleft 1, a very rare congenital anomaly, presents with varying degree of severity from isolated coloboma of the nasal ala to cleft extending upwards (north bound) through the nasal bone into the cranium as Tessier cleft 13.
- 2) Though severe forms are maybe challenging for the reconstructive surgeons, surgical reconstructions involving simpler innovative procedures<sup>2,3</sup> may give satisfactory results in less severe cases.

closed directly after trimming off the dorsal bony hump (Figure 2a-c). The post-operative period was uneventful, and the aesthetic result was satisfactory.

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