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# International Journal of Scientific Study

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# Career Guidance In Medical Education: Is It Mandatory?

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## INTRODUCTION

According to Ivan Prvolesky “career guidance is recognized as training and motivating individuals and students to plan their education, training and work; to take responsibility for their own educational and occupational opportunities, providing help to students for further education, flexible professional development, career management, as well as professional promotion.”<sup>1</sup> It was also said that “career guidance refers to services and activities intended to assist individuals, of any age and at any point throughout their live, to make educational, training and occupational choices and to manage their career.” Such services should be provided at all institutes to enhance the job opportunities for the students and employees which is very much lacking in countries like India. There was no such system existing in Medical Colleges and universities providing continuous career support to the medical students.

## REVIEW OF LITERATURE

Medical council of India amendment 2010 says the guidelines for code of medical ethics, duties and responsibilities of physician, misconduct and punishment and disciplinary action,<sup>2</sup> but there was very least space given to the doctors and medical students to know their career future during their studies in Medical College Institutions. Even in the recently proposed vision 2015 lot of changes have been amended on medical curriculum and competencies to be acquired by a medical graduate during his career as a student, starting right from the foundation course to early clinical exposure, vertical and horizontal integration, competency based learning, emphasis on self-directed learning etc.<sup>3</sup> However, career guidance and counseling was not given a place as a part of the curriculum even by medical council of India Vision 2015 module booklet. It's a known fact that access to career guidance for both undergraduate students and postgraduate specialists has been restricted before. In general, the absence of suitable professional

direction has been well documented.<sup>4</sup> The most specialists report that they have never gotten any career direction or guidance.<sup>5</sup> In an overview of British medical association individuals, comprising of medical students and specialists 95% of respondents reported that they had unmet career guidance requirements.<sup>6</sup> So, the burden on the developing countries about the unmet career direction, and professional development skills will be very much high which was not yet completely known being like an iceberg phenomenon.

## EXPECTATIONS AND SUGGESTIONS

Realizing the pathways in the career that helps in enhancing professional orientation to plan, execute effectively and maintenance of competency is made possible by career information. Expecting career guidance alone does not make any sense. Self-realization of the skills, career pathways, current trends and situation, educational and job perspectives also nurtures your career. Career guidance must be administered by Career Advisors, Professors and senior students. The factors which have immense influence on the effectiveness of career guidance are professional qualifications of career advisors, quality standard information resources on career guidance, accessibility to the available resources and motivation of students with pertinent career education and guidance. Professional qualifications of the personnel's are a major concern. Individuals from different fields cannot guide the students in a proper channel. Career education amenable with curriculum promotes to explore the area of interest and competency assessment and mediates the student to pursue their aspiration.

## SUPPORTS PROVIDED TO STUDENTS TO ASSIST CARRIER GUIDANCE

### Information

1. Introduction to Career guidance to accentuate its importance

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- Orientation programs to be conducted to make certain that students are aware about the importance of the career guidance.

### Resources

Enlightening students with adequate knowledge, materials, staffs, and other aids to function effectively.

- Career Advisors should be invited periodically for guest lectures
- Printed materials must be issued to the students for their future references - like career guidance handbooks
- Accessibility teaching and learning support services that assists for further guidance regarding their career
- Conducting career conferences, forums, focus group discussions, online career programs and discussions.

### Activities

- The students can be encouraged to participate in activities (peer group activities) with relevance to their career interest
- Opportunities should be provided to visit or communicate with organizations and associations outside institution to obtain the information and experience (e.g.: Through research projects, workshops, conferences etc.)
- Motivating students to take responsibilities for their education and work.

At the same time, the career advisors and faculties should have the greater level of competency to assess the outcomes of effective career guidance (Table 1) by following them up in future and having a continuous rapport during professional development.

**Table 1: Outcomes of effective career guidance**

#### Outcomes of effective career guidance

Ability to Integrate and organize the information's obtained from various sources  
 The students must be equipped about their prospects of post-graduation  
 They must be competent to determine their future career and vocational choices  
 They must be able to assess critically about the future practice of medicine and develop the required skills

## CONCLUSION

The author being a member of medical education unit tries to emphasize on the importance of career guidance and counseling should be part of medical curriculum which could be implemented by the medical colleges at their own level with the available faculties and senior professors that will pave the way for our medical graduates to achieve with their maximum potential in the different fields of medical world which we did not get in the past.

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# Effect of Birth Asphyxia on Serum Calcium and Glucose Level: A Prospective Study

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## Abstract

**Background:** Birth asphyxia occipital sinus common cause of mortality and morbidity and associated with various metabolic changes like hypoglycemia and hypocalcemia, hyperkalemia, hyponatremia, hyperphosphatemia. We conducted this study to evaluate changes in serum glucose and serum calcium in birth asphyxia.

**Objective:** To study calcium and glucose levels in asphyxiated newborns of different severity in the early neonatal period and compare with controls.

**Materials and Methods:** Calcium, glucose were estimated in serum samples of asphyxiated newborns of different severity and control group at 24 h of age.

**Results:** The mean serum calcium level at 24 h of age is significantly lower ( $8.31 \pm 0.48$  mg/dl vs.  $9.47 \pm 0.49$  mg/dl;  $P < 0.001$ ), mean serum glucose level was significantly lower ( $54.4 \pm 10.91$  mg/dl vs.  $76 \pm 15.5$  mg/dl;  $P < 0.001$ ) in cases than control group. Among cases there was significant negative correlation of serum calcium level and severity of asphyxia ( $P < 0.01$ ) while there was highly significant positive correlation of serum calcium with period of gestation (POG) and birth weight ( $P < 0.01$ ). In the present study, there was a significant negative correlation of serum glucose level and severity of asphyxia ( $P < 0.01$ ) whereas highly significant positive correlation was there of serum glucose with POG and birth weight.

**Conclusion:** In the present study, it has been concluded that in birth asphyxia, there is highly significant fall in serum calcium and glucose as compared to controls and proportional to degree of asphyxia.

**Key words:** Apgar score, Birth asphyxia, Hypocalcemia, Hypoglycemia, Serum calcium, Serum glucose

## INTRODUCTION

World Health Organization has defined birth asphyxia as “failure to initiate and sustain breathing at birth.”

Perinatal asphyxia one of the most common primary cause of mortality (28.8%) and morbidity among neonates in India and is the commonest cause of stillbirths (45.1%). An Apgar score of  $<7$  at 1 min and at 5 min respectively is seen in 8.4% and 2.45% cases in India.<sup>1</sup>

The primary cause of this condition is systemic hypoxemia and/or reduced cerebral blood flow. Birth asphyxia causes 23% of all neonatal death worldwide.

Birth asphyxia is associated frequently with metabolic changes like hypoglycemia, hypocalcemia, hyponatremia, hyperphosphatemia and metabolic acidosis. Calcium is an important second messenger in our body and also helps out muscle function and acts as a co-factor for several enzymatic activities. During pregnancy, calcium is transferred actively from the maternal circulation to the fetus by a transplacental Ca pump regulated by the parathyroid hormone-related peptide. The majority of fetal Ca accretion occurs in the third trimester. This process results in higher plasma Ca concentration in fetus than in the mother and leads to fetal hypocalcemia with total and ionized Ca concentration of 10-11 mg/dl and 6 mg/dl in umbilical cord blood at term.<sup>2</sup>

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After birth due to the abrupt cessation of placental transfer of calcium hence, levels starts falling to 8-9 mg/dl and ionized calcium to 4.4-5.4 mg/dl at 24 h of age. Serum calcium then starts rising to reach levels comparable to older children and adults by 2 weeks of age.<sup>3</sup>

Glucose is an essential nutrient for the brain. Abnormally low level can cause encephalopathy and have the potential to produce long-term neurological injury. Serum glucose levels decline after birth until 1-3 h of age, when levels spontaneously increase in normal infants. In healthy term infants, serum glucose values are rarely <35 mg/dl between 1 and 3 h of life, <40 mg/dl from 3 to 24 h and <45 mg/dl after 24 h of life.<sup>4</sup> In birth asphyxia, hypoglycaemia is due to glycogen depletion secondary to catecholamine release and to an unexplained hyperinsulinemic state. An initial phase of hyperglycemia and hypoinsulinemia (5-10 min following an acute event due to a catecholamine surge which inhibits insulin release and stimulates glucagon release) may be followed within 2-3 h by profound hypoglycaemia.<sup>5</sup>

This study was undertaken to detect the incidence of hypocalcemia and hypoglycemia in asphyxiated babies as to prevent the adverse effects of these biochemical abnormalities in the newborns.

## MATERIALS AND METHODS

The study was conducted on 100 newborns delivered in the obstetrics department and admitted to neonatology section of Department of Pediatrics, Government Medical College/Rajindra Hospital, and Patiala.

In a series of 135 newborns selected, 100 newborns were asphyxiated, and 35 served as control group. The study was approved by the Institutional Ethical Committee, and informed consent was obtained from the parents of each subject. In this study, 100 asphyxiated neonates (Apgar score at 1 min 7 or less) were taken as cases of study. 35 normal neonates (Apgar score at 1 min more than 7) were taken as control. Total serum calcium and serum glucose levels were determined at 24 h of life in all the newborns. Serum calcium was estimated by O-Cresolphthalein complex one end point (kit) method (Connerty and Briggs, 1966).<sup>6</sup> Blood glucose estimation was done by Asatoor and King Method.<sup>7</sup> Babies with congenital malformations, serum creatinine levels more than 1.5 mg/dl, suspected metabolic disease, treated with diuretics and those born to mothers having hypertension, diabetes mellitus, toxemia of pregnancy were excluded from the study.

## RESULTS

Of the 100 cases, 55 were male newborns and 45 were females, mean birth weight in the study group was 2405.70 ± 638.32 g, 36 newborns were delivered by normal vaginal delivery, 62 were lower segment caesarean section. The study group was comprised of 53 cases of mild birth asphyxia, 26 cases of moderate birth asphyxia and 21 cases of severe birth asphyxia.

In 35 control group, 18 were males and 17 newborns were female newborns, mean birth weight was 2624.28 ± 555.76 g respectively. 29 newborns were delivered by normal vaginal delivery, 6 were by lower segment caesarean section.

Statistical comparison of measured values between two groups were performed by the unpaired *t*-test of the means and ANOVA test of the groups. It was found that mean calcium levels in the study and control group were 8.31 ± 0.48 and 9.47 ± 0.49 mg/dl. The mean serum calcium level in the study group was lower as compared to control group, and statistical difference was highly significant (*P* < 0.001) as shown in Figure 1. In present study, mean calcium level of severely asphyxiated babies 7.96 ± 0.91 mg/dl was significantly lower than mean calcium level of mild and moderately asphyxiated babies 8.50 ± 0.50 mg/dl and 8.21 ± 0.38 mg/dl (*P* < 0.05), mean calcium level of moderately asphyxiated newborns were lower than mildly asphyxiated newborns (*P* < 0.05) as shown in Figure 2. This shows that calcium levels at 24 h of life is related to severity of asphyxia indicating that serum calcium has negative correlation with severity of asphyxia and highly significant positive correlation with period of gestation (POG) and birth weight as shown in Table 1.

In the present study, mean glucose levels of the study and control groups were 54.4 ± 10.91 and 76 ± 15.5 mg/dl. The mean serum glucose level in the study was lower as compared to control group, and the statistical difference was highly significant (*P* < 0.001) as shown in Figure 3. It was found that mean glucose level of severely asphyxiated babies 46.8 ± 4.58 mg/dl was significantly lower than

**Table 1: Co-efficient of correlation between serum calcium and other parameters**

Parameter	Coefficient of correlation	<i>P</i> value	Significance	Regression equation Y=a+bx
Serum calcium	-	-	-	-
Asphyxia	-0.45	<0.01	S	-0.39x+4.22
POG	+0.48	<0.01	HS	0.079x-5.40
Birth weight	0.47	<0.01	HS	0.0003x+7.469

POG: Period of gestation

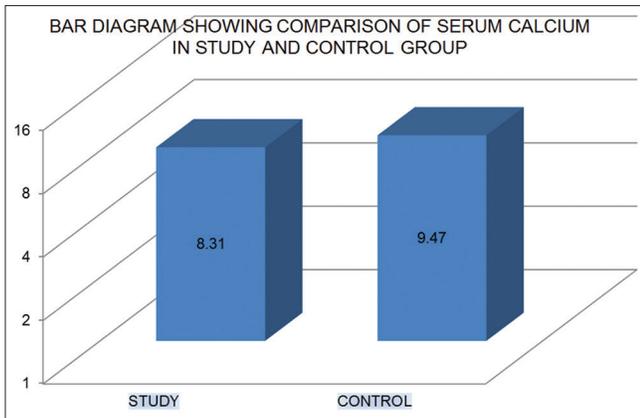


Figure 1: Serum calcium in study and control group

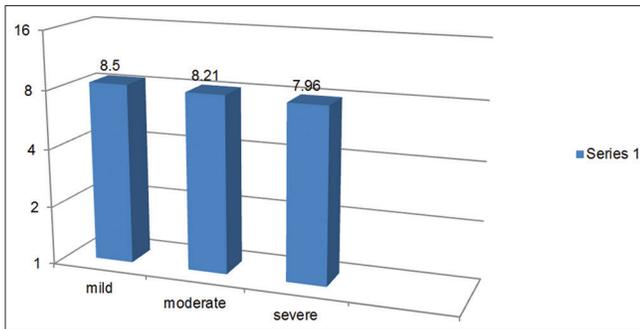


Figure 2: Serum calcium in study group according to severity of asphyxia

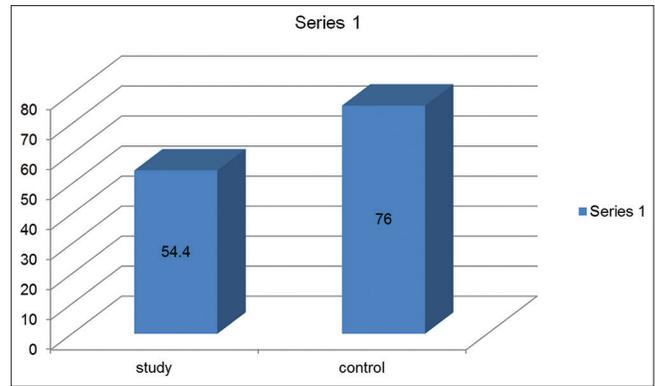


Figure 3: Glucose levels in study and control group

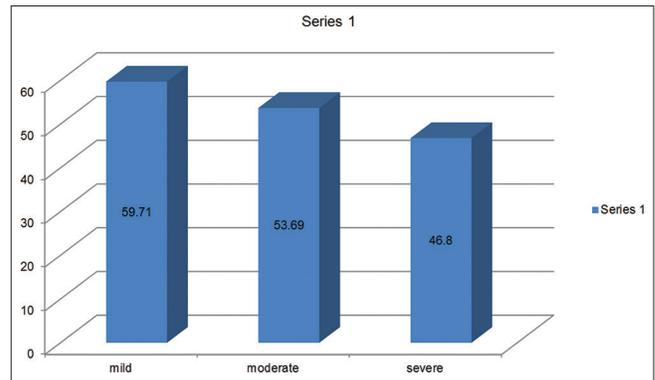


Figure 4: Glucose levels according to grades of asphyxia

mean glucose level of mild and moderately asphyxiated babies  $59.71 \pm 11.47$  mg/dl and  $53.69 \pm 6.97$  mg/dl ( $P < 0.05$ ), mean glucose level of moderately asphyxiated newborns were lower than mildly asphyxiated newborns ( $P < 0.05$ ). This shows that glucose levels at 24 h of life was inversely related to severity of asphyxia. ( $P < 0.05$ ) as shown in Figure4. Serum glucose level had significant positive correlation with POG and birth weight ( $P < 0.01$ ) and significant negative correlation with asphyxia as shown in Table 2.

Table 2: Co-efficient of correlation between serum glucose and other parameters

Parameters	Coefficient of correlation	P value	Significance	Regression equation Y=a+bx
Serum glucose	-	-	-	-
Asphyxia	-0.50	<0.01	S	-6.93x+67.58
POG	+0.40	<0.01	HS	1.56x-1.497
Birth weight	+0.35	<0.01	HS	0.006x+41.30

POG: Period of gestation

## DISCUSSION

Perinatal asphyxia is a common neonatal problem and contributes significantly to neonatal mortality and morbidity. Hypoxic ischemic brain injury is the most important consequence of perinatal asphyxia.

Out of 100 cases, 44 babies had fetal asphyxia as well. Babies with Apgar score  $\leq 7$  were defined as asphyxiated and babies with Apgar score more than 7 constituted the control, group. All the neonates (both study group and control group) were subjected to determination of total serum calcium and glucose at 24 h of life. In the present study, it was found that there was a significant decrease in

the extracellular calcium levels in the asphyxiated babies, and the decrease was directly proportional to the degree of asphyxia. This is similar to that reported by Manzke and Kruse who estimated total calcium and ionized calcium in asphyxiated as well as non-asphyxiated newborns and concluded that the decrease in the serum level of both the total calcium and the ionized calcium was more in asphyxiated newborns than non-asphyxiated newborns.<sup>8</sup> Jajoo *et al.* has also observed the high incidence of low serum calcium in asphyxiated infants.<sup>9</sup> According to a study conducted by Schedewie *et al.*, asphyxiated infants exhibited significantly low plasma calcium concentrations than their controls.<sup>10</sup> The present study shows that level of calcium at 24 h of life is related to severity of asphyxia indicating

that serum calcium has negative correlation with severity of asphyxia ( $P < 0.01$ ) while there was highly significant positive correlation with POG and birth weight. This is in accordance with study by Mimouni *et al.* and Basu *et al.* who concluded that low serum calcium values were significantly associated with low gestational age and low Apgar score.<sup>11,12</sup>

In the present study, it was found that there was a significant decrease in the serum glucose in asphyxiated babies and decrease was directly proportional to the degree of asphyxia. This is similar to that observed by Xu *et al.* and Davis *et al.*, Xu *et al.* observed in their study, at day 1 of life, in asphyxiated neonates that temporary hyperinsulinism contributed to hypoglycaemia in these babies.<sup>13</sup> Davis *et al.* had also reported in their study that there was hypoglycaemia due to severe asphyxia.<sup>14</sup> Singhal *et al.* in their study concluded that out of 2/3 hypoglycemic babies, birth asphyxia contributed to 24.2% of cases.<sup>15</sup> The present study showed that there was significant negative correlation between serum glucose level and severity of asphyxia ( $P < 0.01$ ) whereas highly significant positive correlation was there of serum glucose with POG and birth weight ( $P < 0.01$ ).

## CONCLUSION

It can be concluded from the present study that with perinatal asphyxia, develops hypocalcemia (when serum calcium levels  $<7$  mg/dl) and hypoglycaemia (when serum glucose  $<40$  mg/dl) after birth in proportion to severity of asphyxia and severely asphyxiated babies develop hypoglycaemia and hypocalcemia which may require medical intervention.

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# Comparison of Ramosetron and Palonosetron for Control of Post-operative Nausea and Vomiting following Middle Ear Surgeries: A Prospective Randomized Double-blind Study

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## Abstract

**Background:** Post-operative nausea vomiting (PONV) is a distressing complaint particularly in high-risk patients. 5-HT<sub>3</sub> receptor antagonists has proved a promising role in the prophylaxis of PONV.

**Aim:** We aim to compare the anti-emetic responsiveness of ramosetron and palonosetron in post-operative patients of middle ear surgeries.

**Materials and Methods:** In the present randomized, prospective double-blind study is including 60 American Society of Anesthesiology Grade I/II female patients, between 25 and 40 years of age undergoing elective middle ear surgeries. Patients were divided into two groups; Group R: Injection ramosetron 0.3 mg (intravenous [IV]) in 2 ml solution and Group P: Injection palonosetron 0.075 mg (IV) made 2 ml after adding 0.5 ml normal saline, were administered for prevention of PONV in the present study. The study drugs were administered before shifting of the patient from the operating room to the post anesthesia care unit. The efficacy, as well as side effects of ramosetron and palonosetron was documented and compared.

**Results:** In the present study, the complete response was observed in 90.91% and 70.91% of the patients observed during 0-2 h and 2-24 h respectively in Group R while in Group P no PONV was found in 92.73% and 80% of the patients within the same time frame ( $P > 0.05$ ). However, during 24-48 h significant complete response was observed among both the groups ( $P = 0.03$ ). Severity of nausea, retching and vomiting was also found to be significantly high in ramosetron group as compared to the patients received palonosetron. Total rescue antiemetic was given more among ramosetron group. However, no significant difference was observed when compared with palonosetron group ( $P = 0.11$ ).

**Conclusion:** Palonosetron was found an effective and better antiemetic than ramosetron in patients undergoing middle ear surgeries.

**Key words:** Palonosetron, Post-operative nausea vomiting, Ramosetron, Serotonin 5-HT<sub>3</sub> receptor antagonists

## INTRODUCTION

Post-operative nausea and vomiting (PONV) is a common complaint among the patients of middle ear surgeries

with a reported incidence of 62-80%.<sup>1-3</sup> PONV at times is more distressing than post-operative pain and can further complicate post-operative care in several ways like electrolyte disturbance and dehydration, aspiration of vomitus and wound dehiscence due to frequent expulsive efforts, associated with delayed recovery and prolonged hospital stay.<sup>4</sup> Middle ear surgeries stimulate the vestibular system thereby increases the incidence of nausea and vomiting.<sup>5</sup> The introduction of 5-HT<sub>3</sub> antagonists in medical era is a milestone for promoting day care surgery and anesthesia. These drugs are very commonly used now a days, with more safety and favorable side-effects profile

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as they lack the extra-pyramidal, dysphoric, sedative and side effects of other commonly used antiemetics.

Ondansetron is the most favored drug among the medical professionals and is being routinely used either alone or in combination with other drugs, for the prophylaxis of PONV in day care surgery. A newer drug, ramosetron, is a recently developed selective 5-HT<sub>3</sub> receptor antagonist. It exhibits significantly greater 5-HT<sub>3</sub> receptor binding affinity with slow dissociation rate thus implying better potency and longer receptor antagonizing effects compared with Ondansetron.<sup>6</sup> Thereafter, palonosetron (“second-generation” 5-HT<sub>3</sub> receptor antagonist with a mean elimination half-life of about 40 h) is introduced possessing the property of even better receptor-binding affinity than the “first generation” 5-HT<sub>3</sub> antagonists.<sup>7,8</sup> Moreover, it also have a property to bind to the receptor at an allosteric site different from those that bind ondansetron and granisetron.<sup>7</sup>

Extensive Medline search revealed a number of studies comparing the efficacy of ramosetron and palonosetron on PONV, but controversy still persists regarding the best suitability of the drug for day care anesthesia. Moreover, lack of comparative studies between these two drugs in developing countries and limited availability of literature regarding the use of these drugs for middle ear surgeries compelled us to perform our study. Therefore, we designed a prospective randomized study to compare the efficacy of ramosetron and palonosetron in preventing PONV for the patients undergoing middle ear surgeries.

## MATERIALS AND METHODS

After approval from the Institutional Ethical Committee and written informed consent, we conducted a study including 60 American Society of Anesthesiology Grade I/II female patients, between 25 and 40 years of age undergoing elective middle ear surgeries in Teerthankar Mahaveer Medical College from November 2014 to April 2015. Patients with history of drug abuse, body mass index >35, patients on chronic steroid therapy, and patients with diabetes mellitus or cardiovascular disease, history of motion sickness, gastrointestinal disease was excluded from the study.

A consultant anesthesiologist assessed all patients during pre-anesthetic evaluation and alprazolam (0.5 mg) orally was prescribed in all patients on the night before surgery and advised nil per orally from midnight. Before reaching the operating room (OR) a good intravenous (IV) access was secured with 20 G cannula and preloading was done with 10 ml/kg of ringer lactate solution. Monitoring devices for ECG, heart rate, oxygen saturation and end-tidal carbon dioxide were attached.

Randomisation was performed by computer generated program and the patients were allocated in two groups of 55 patients each. Group R: Injection ramosetron 0.3 mg (IV) in 2 ml solution and Group P: Injection palonosetron 0.075 mg (IV) made 2 ml after adding 0.5 ml normal saline, were administered for prevention of PONV in the present study. Drugs were prepared by a blinded anesthesia technician not involved in the study in identical 5 ml syringes and were administered according to the randomization list.

A well-defined anesthesia regimen was used in all the patients that included induction with injection propofol 2 mg/kg (IV) and injection fentanyl 1 µg/kg (IV). Intubation was facilitated by using injection vecuronium 0.1 mg/kg (IV). After confirming correct placement of endotracheal tube by capnography, we secured a nasogastric tube. Maintenance of anesthesia was done using nitrous oxide (66%) and isoflurane (1-2%) in oxygen. Intra-operative muscle relaxation was maintained with intermittent doses of injection vecuronium. At the end of the surgery, injection diclofenac 75 mg (intramuscular) was given and reversal of neuromuscular blockade was performed with injection neostigmine 0.05 mg/kg (IV) and Injection glycopyrrolate 0.1 mg/kg (IV). After thoroughly doing the oral/nasogastric suction, patients were extubated in a fully awake state. Ramosetron 0.3 mg or palonosetron 0.075 mg was administered IV before shifting of the patient from the OR to the post-anesthesia care unit (PACU). No opioids were given for post-operative analgesia at any point of time. In the PACU, patients were monitored for nausea, retching, vomiting, pain, vital signs, and post-anesthetic discharge score. Patients were closely monitored for 48 h and any complaint of nausea, retching, and vomiting or adverse drug effect was recorded by an independent observer who was blinded to the study.

Nausea was defined as a subjectively unpleasant sensation associated with awareness of the urge to vomit whereas retching was defined as the labored spasmodic, rhythmic contraction of the abdominal muscles without expulsion of gastric contents, and vomiting was defined as the forceful expulsion of gastric contents from the mouth.<sup>9-11</sup> Rescue antiemetic (not belonging to the 5-HT<sub>3</sub> receptor antagonist group, i.e. metoclopramide 10 mg) was given if two or more episodes of emesis occurred in each observation period. We made no distinction between vomiting and retching for treatment purpose. A trained nurse taking care of the patient and blinded to the study recorded all episodes of PONV (nausea, retching, and vomiting) either by direct questioning or by spontaneous complaint by the patients during three periods within the first 48 h after anesthesia: 0-2 h in the PACU, 2-24 h in the general ward and 24-48 h also in the general ward. Nausea was scored

on an 11-point verbal rating scale from 0 (no nausea) to 10 (worst possible nausea): Severity was scored as mild (1-3), moderate (4-6), or severe (7-10).<sup>12</sup> Any side effects/adverse effects were recorded during the study period by the attending anesthesiologist and otolaryngorhinologist. Patient satisfaction regarding their satisfaction to be free of nausea and vomiting was performed on a four-point Likert scale (dissatisfied, neutral, satisfied, and highly satisfied) at the completion of the study.<sup>8</sup>

**Statistical Analysis**

Sample size was predetermined using a power analysis to achieve an 80% chance (b = 0.2) of detecting a 40% reduction in PONV from a basal incidence of 70% (from 70% to 42%) with an assumed significance level of a = 0.05.<sup>13</sup> A minimum number of 49 patients in each group were calculated and considering 10% attrition rate we included 55 patients in each group. Data analysis was performed using SPSS, version 19 (SPSS Inc., USA). All the statistical tests were two-tailed. All the values were expressed as mean ± standard deviation. A P < 0.05 was considered as significant.

**RESULTS**

All patients were successfully enrolled and underwent middle ear surgery in our study without any dropouts. The ramosetron group and the palonosetron group were comparable with respect to patient’s demographic data, duration of surgery/anesthesia (Table 1).

The complete response was observed in 90.91% and 70.91% of the patients during 0-2 h and 2-24 h respectively in Group R while in Group P no PONV was found in 92.73% and 80% of the patients within the same time frame (P > 0.05) (Table 2). However, during 24-48 h significant complete response was observed among both the groups (P = 0.03). Nausea severity was more in Group R as compared to Group P, and significant difference was observed during 2-24 h (P = 0.05) and 24-48 h (P = 0.01). Episodes of retching was also found to be significant during 2-24 h and 24-48 h among Group R (14.55% and 27.28%) as compared to Group P (3.63% and 7.28%) (P = 0.04 and 0.001). During first 24 h frequency of vomiting was comparable among the two groups. However, during 24-48 h we observed significant increase in the episodes of vomiting in Group R (P = 0.04) (Table 2). Total rescue antiemetic was given more among ramosetron group, however no significant difference was observed when compared with palonosetron group (P = 0.11). On enquiry with the patients 17 patients advocated satisfaction with ramosetron while 24 patients were satisfied with palonosetron (P = 0.20) (Table 2).

Transient dizziness, dyspepsia, headache, weakness and flushing/erythema were noted in 1, 2, 4, 4, and 5 patients, respectively, in Group R, while the same was observed in 1, 1, 5, 1, and 3 patients in Group P (Table 3). The flushing/erythema at the site of injection was non-tender that subsided on its own without requiring any treatment over the next 24 h (Table 3).

**DISCUSSION**

In middle ear surgeries, continuous drilling and irrigating the bone causes vestibular stimulation leading to a distressing problem of PONV.<sup>14</sup> The incidence of PONV after general anesthesia is 20-30% and it becomes more

**Table 1: Demographic variables (mean±SD)**

Characteristics	Group R	Group P	P value
Age (years)	29.82±4.62	28.87±3.74	0.23
Height (cm)	153.64±3.51	154.27±2.87	0.30
Weight (kg)	53.65±4.47	54.52±5.21	0.35
Duration of surgery (min)	126.75±7.92	129.54±8.89	0.10
Duration of anesthesia (min)	131.61±8.64	133.62±9.83	0.26

SD: Standard deviation

**Table 2: Comparison of frequency of nausea, retching and vomiting episodes in patients administered ramosetron and palonosetron**

Variables	Groups	Events frequency (n (%))		
		0-2 h	2-24 h	24-48 h
Complete response	Group R	50 (90.91)	39 (70.91)	29 (52.73)
	Group P	51 (92.73)	44 (80.00)	40 (72.73)
	P value	0.72	0.26	0.03*
Nausea severity (mild, moderate, severe)	Group R	1/2/1	4/9/6	5/8/7
	Group P	1/1/1	2/4/4	3/4/2
	P value	0.69	0.05*	0.01*
Retching	Group R	3 (5.46)	8 (14.55)	15 (27.28)
	Group P	1 (1.81)	2 (3.63)	4 (7.28)
	P value	0.3	0.04*	0.001*
Vomiting	Group R	4 (7.28)	11 (20.00)	17 (30.91)
	Group P	3 (5.46)	6 (10.91)	8 (14.55)
	P value	0.69	0.18	0.04*
Total rescue antiemetic given (no. of patients)	Group R	25 (45.46)		
	Group P	17 (30.91)		
	P value	0.11		
Overall satisfaction (dissatisfied/neutral/satisfied/highly satisfied)	Group R	28/10/10/7		
	Group P	19/12/16/8		
	P value	0.20		

\*P<0.05

**Table 3: Adverse events in number (percentage)**

Adverse event	Group R	Group P
Dizziness	1 (1.81)	1 (1.81)
Dyspepsia	2 (3.63)	1 (1.81)
Headache	4 (7.28)	5 (5.46)
Weakness	4 (7.28)	1 (1.81)
Flushing	5 (5.46)	3 (7.28)

worrisome after gynecologic, laparoscopic, breast and middle ear surgeries.<sup>15</sup>

Many consensus guidelines were proposed in the past to eliminate the problem of PONV. The recent introduction of palonosetron together with its greater 5-HT<sub>3</sub> receptor binding appealed many researchers to choose this drug in their studies. Bicer *et al.*<sup>16</sup> performed a study to compare different doses (0.5, 1.0, and 1.5 µg/kg) of palonosetron in pediatric patients undergoing strabismus surgery and recommended further evaluation as all appeared effective doses. However, FDA has now established that the minimum effective dose of palonosetron for the prevention of PONV is 0.075 mg.<sup>17,18</sup> Hence, we choose the same dose of palonosetron for our study.

The complete response (patients with no PONV) was seen more in the patients given palonosetron than ramosetron group, although the results were comparable among them during 0-2 h and 2-24 h' time period. However, after 24-48 h postoperatively 52.73% of the patients of Group R had complete response whereas 72.73% of the patients did not complain of PONV of Group P ( $P = 0.03$ ). The better outcome after 24 h shown by the patients given palonosetron might be because of the greater half-life of palonosetron (40h) as compared to patients received ramosetron. This is similar to various studies that the palonosetron was observed as better long duration effect than ramosetron.<sup>12,19,20</sup> In a comparative study done by Fujii *et al.*,<sup>21</sup> they observed a complete response in 90% of the patients in ramosetron group while 86% in patients who were given Granisetron. During 24-48 h after surgery, a complete response was observed in ramosetron and Granisetron group as 90 and 66%, respectively. Oshima *et al.*<sup>22</sup> found that 30 mg of TandoSPIRONE imparted a complete response in 67% of the patients. Various researchers also observed similar effectiveness of ramosetron in their studies during the first 24 h postoperatively, although they compared the drug with Ondansetron.<sup>6,23</sup>

The patients received ramosetron experienced more severe grade of nausea than those of patients given palonosetron from 2 to 48 h. Chattopadhyay and Goswami<sup>19</sup> supports our study in which they also observed that severity of nausea was statistically significant with ramosetron group within 2-48 h postoperatively. In high-risk patients, after thyroidectomy palonosetron proved to be more effective than ondansetron especially 2-24 h after surgery.<sup>14</sup>

We have also included the episodes of retching in our study in which the effectiveness of palonosetron is evident as the patients received ramosetron suffered from more episodes of retching 2 h postoperatively. Such findings are not observed by most of the researchers of PONV in their studies.

In terms of vomiting, although more number of patients experienced vomiting in ramosetron group but significant difference was not observed during the first 24 h. Due to better receptor binding to an allosteric site and slow dissociation property of palonosetron receiving patients, the episodes of vomiting rises significantly in ramosetron group 24-48 h after surgery. As the episodes of vomiting are higher in ramosetron group, therefore, the requirement of rescue emetic is more in Group R than Group P ( $P = 0.11$ ). The persistent beneficial effect of palonosetron as compared to ramosetron could be explained from the fact that the former drug has a prolonged elimination half-life.<sup>8</sup> So, palonosetron is a better effective alternative than ramosetron after first post-operative day.

Upon enquiring the patient satisfaction score by Likert scale, palonosetron better fulfilled the satisfaction score than ramosetron and it can be explained by the fact that during our study better results are observed with Group P patients than Group R.

In the present study, a significant number of adverse effects was also noted among both the groups. However, all adverse effects were uneventful and successfully managed.

Another possible mechanism for PONV could be the use of Nitrous oxide during intra-operative period. We have used Nitrous oxide in our cases due to financial constraints of our hospital. However, use of short-acting opioid or a continuous propofol infusion might be a better option.<sup>24-26</sup>

### Limitations

In the present study, a control group should be there whereby we can observe PONV at a basal level but post-operative patients of middle ear surgery is itself prone to higher chances of PONV and in such situation giving them a placebo would be injustice and unethical to those patients. Secondly, ramosetron has a short half-life than palonosetron and in such circumstances the dosing schedule for ramosetron should be multi-regimen but including more dosing schedules of ramosetron would lead to bias in the study. Thirdly, we have given Fentanyl during induction of anesthesia, being an opioid it can exaggerate PONV. However, in recent study it is observed that pain treated with opioids actually prevents PONV.

### CONCLUSION

The present study clearly states that palonosetron is a better and effective alternative for PONV in middle ear surgeries during the first and second post-operative day. A good patient's satisfaction and a prolong duration of anti-emetic cover advocates its use in patients undergoing middle ear surgeries in general anesthesia.

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# Prevalence of Anxiety in Schizophrenic Patients and its Impact on Quality of Life

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## Abstract

**Introduction:** Anxiety symptoms commonly co-occur in patients of schizophrenia and have significant deleterious influence on course of schizophrenic illness and overall prognosis.

**Aim:** To study prevalence of anxiety in patients suffering from schizophrenia.

**Objectives:** (1) To investigate, the prevalence of co-occurring anxiety and severity of anxiety in relation to schizophrenia. (2) To study, the impact of anxiety symptoms on quality of life (QOL) of schizophrenic patients.

**Materials and Methods:** The patients suffering from schizophrenia were randomly selected from outpatient and inpatient department of psychiatry from Medical College and Hospital. Sample size of 60 patients was administered different psychometric scales for profiling schizophrenic symptoms, measurement of anxiety symptoms, and measurement of QOL.

**Results:** Among the patients 66.67% patients were having at least one anxiety symptom. The prevalence of anxiety disorders was 48.33%. Anxiety disorders were more common in paranoid subtype (57.7%) as compared to non-paranoid subtype and were more commonly (62.06%) associated with early schizophrenia i.e., illness <2 year duration. The majority were having social anxiety 2<sup>nd</sup> common was panic disorder and followed by obsessive-compulsive disorder. Furthermore, overall QOL of schizophrenic patient was significantly impaired when co-morbid anxiety is detected.

**Conclusion:** It is clearly evident that the patients with schizophrenia have high prevalence of anxiety. Proper psychiatric screening and detailed evaluation is required, so that anxiety is detected early and treated for improvement of prognosis of schizophrenia and improving QOL of schizophrenic patients.

**Key words:** Anxiety, Prevalence, Prognosis, Quality of life, Schizophrenia

## INTRODUCTION

Schizophrenia is a group of brain disorders characterized by symptoms such as hallucinations, delusions, disorganized communication, poor planning, reduced motivation, and blunted affect.<sup>1</sup> These symptoms cause major bulk of disability in such patients. Further adding to our confusion toward the clinical picture of schizophrenia, anxiety symptoms are also frequently observed.

Some studies have suggested that anxiety in schizophrenic patients might be associated with both positive<sup>2</sup> and negative<sup>3</sup> symptoms. In addition, extrapyramidal symptoms that develop secondary to neuroleptic treatment may also be co-exist with anxiety symptoms.<sup>4</sup>

Anxiety symptoms or disorders in schizophrenic patients are significant, as they increase the risk of recurrence and suicide and impair social and professional functions and quality of life (QOL).<sup>5,6</sup>

Comorbid anxiety disorders or symptoms such as obsessive-compulsive disorder (OCD), panic disorder, social phobia, and generalized anxiety disorder (GAD), and posttraumatic stress disorder (PTSD) can develop in schizophrenia in the same way as in patients with anxiety disorder only.<sup>7</sup>

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The purpose of this study is to add to knowledge about severity of anxiety symptoms in patients with schizophrenia and to guide the mental health professionals to better understand the diagnosis and treatment of anxiety symptoms in patients with schizophrenia.

**Aim**

To study, the prevalence of anxiety in patients suffering from schizophrenia.

**Objectives**

1. To investigate, the prevalence of co-occurring anxiety symptoms and their severity in patients suffering from schizophrenia.
2. To study, the impact of anxiety symptoms on QOL in patients suffering from schizophrenia.

**MATERIALS AND METHODS**

This observational study was cross-sectional in nature, carried out on 65 patients from September 2012 to September 2014 approximately for 2 years in Psychiatry Department of a Medical College Hospital. Schizophrenic patients reporting to Psychiatry Department were recruited after taking informed consent.

The study was approved by the Ethical Committee of Medical College and Hospital.

**Inclusion Criteria**

1. Patients diagnosed as schizophrenia according to Diagnostic and Statistical Manual of Mental Disorders, 4<sup>th</sup> Edition, Text Revision (DSM-IV-TR)
2. Patients of more than age of 18 years up to 60 years.

**Exclusion Criteria**

1. Patients with co-morbid medical illness
2. Patients with use of any psychotropic substances
3. Patients who have received electro convulsive therapy within last 6 months
4. Patients who have drug induced side effects.

The socio demographic profile and clinical variables were recorded in specific case report form prepared for this clinical study. All the patients underwent thorough clinical examination.

At the time of interview, following instruments or psychometric scales were administered for approximately 60-90 min session:

1. Duke health profile<sup>8</sup>
2. DSM-IV-TR criteria and Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I)<sup>9</sup>
3. Positive and negative syndrome scale (PANSS)<sup>10</sup>

The patients after administration of sociodemographic data and SCID-I were then administered Dukes health profile for screening of patients for anxiety. Then patients were divided according to score into anxiety screening positive patients and anxiety screening negative patients.

Patients who were positive on anxiety screening were then administered Hamilton anxiety (HAM-A)<sup>11</sup> to estimate severity of anxiety in these patients. After that WHO QOL-BREF<sup>12</sup> scale was administered on all patients and data collected.

Each case was evaluated and discussed with senior psychiatrist and diagnose as per DSM-IV TR criteria. Furthermore as per DSM-IV-TR criteria patients were identified, and diagnosed as having specific subtype of schizophrenia. Then, relation of anxiety and severity of anxiety with all variable of schizophrenia were studied and evaluated. Furthermore relation of anxiety with socio demographic data of patients suffering from schizophrenia was evaluated. Medical data were obtained from subjects and from their medical records.

**Statistical Analysis**

The results obtained were analyzed using the Chi-square test, ANNOVA test and statistical methods. The Chi-square test was applied on obtained data to test the significance of difference between two proportions.

**RESULTS**

This study consisted of 65 patients out of that 5 patients refused to complete the psychometric scales and questionnaire. Thus, these 5 patients were eliminated, which left 60 patients in this study. Among the patients 66.67% ( $n = 40$ ) patients were having at least one anxiety symptom and the prevalence of anxiety disorder was 48.33% ( $n = 29$ ) (Table 1 and Graph 1).

Among 29 schizophrenic patients diagnosed with anxiety, majority, i.e., 57.7% ( $n = 23$ ) had paranoid schizophrenia (Table 2 and Graph 2).

This study further divided patients according to degree of severity of anxiety by applying HAM-A scale and it was

**Table 1: Anxiety distribution according to screening scale (Dukes health profile) among the patients suffering from schizophrenia**

Anxiety on screening test	Number of patients	Percentage
Screening positive	29	48.33
Screening negative	31	51.66
Total	60	100

found that 26 out of 29 patients (89.65%) had moderate to severe degree of anxiety.

Anxiety disorders were found to be more prevalent in schizophrenic patients with predominant positive symptoms (Table 3 and Graph 3) and were more common in early schizophrenia, i.e., illness duration <2 years (Table 3).

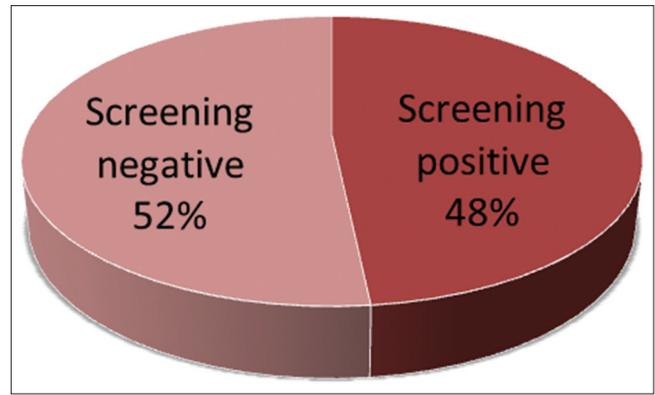
Overall QOL of schizophrenic patient was significantly impaired when co-morbid anxiety is detected (Table 4).

Total six types of anxiety disorders were found in 29 schizophrenic patients with co-morbid anxiety.

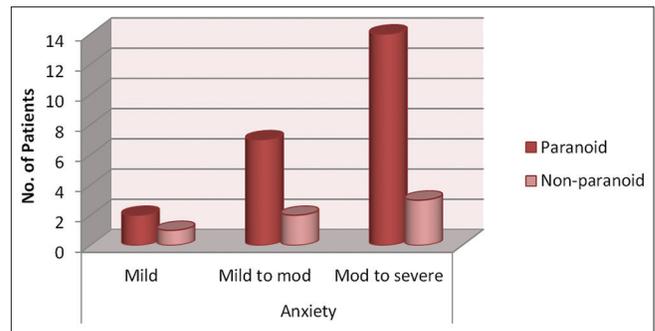
As in Table 5, majority schizophrenic patients were having social anxiety (31.03%), 2<sup>nd</sup> common was panic disorder (24.13%) and followed by OCD (20.68%).

**DISCUSSION**

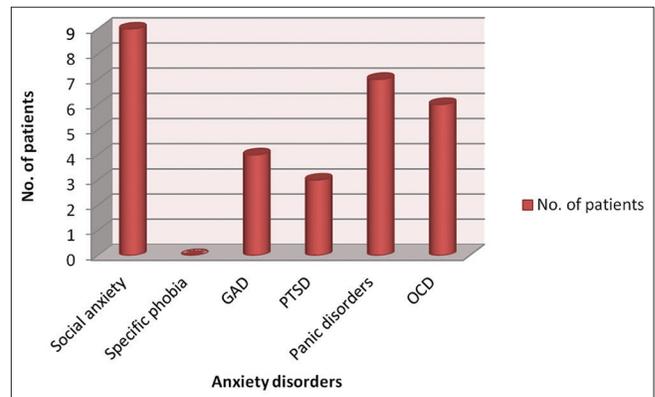
Though the recognition of co-occurrence of anxiety disorders in schizophrenia dates back to the early years of psychiatric nosology, the topic has long been neglected in both research, and clinical settings. Studies have demonstrated that anxiety disorders are commonly found in schizophrenic patients and they have significant influence on course of illness, its impact on day to day functioning of the patient and overall prognosis. Recognizing and



Graph 1: Number of patients by anxiety screening test



Graph 2: Severity of anxiety a/c subtype of schizophrenia



Graph 3: Anxiety disorders

**Table 2: Anxiety and its severity distribution according to subtypes of schizophrenia among patients of schizophrenia**

Schizophrenia subtypes	Anxiety (%)			Total patient having comorbid anxiety
	Mild	Mild to moderate	Moderate to severe	
Paranoid	2 (8.67)	7 (30.43)	14 (60.87)	23 (57.50)
Non-paranoid	1 (16.66)	2 (33.33)	3 (50)	06 (30)
Total	3 (10.34)	9 (31.03)	17 (58.62)	29

**Table 3: Distribution of anxiety and its severity according to duration of schizophrenia and PANSS score among patients suffering from schizophrenia**

Anxiety disorders (%)	Duration in years of schizophrenic illness			Total	PANSS score: Prominent symptoms		
	<2	3-10	>10		Points with predominant positive symptoms	Points with predominant negative symptoms	General psycho-pathology
Absent	8 (25.80)	13 (41.93)	10 (32.25)	31	10 (32.25)	12 (38.70)	09 (29.03)
Present	18 (62.06)	9 (31.03)	2 (6.89)	29	20 (68.96)	6 (20.68)	3 (10.34)
Mild	0	3 (100)	0	3	3 (100)	0	0
Mild-moderate	3 (33.33)	4 (44.44)	2 (22.22)	9	6 (66.66)	1	2 (22.22)
Moderate-severe	15 (57.69)	2 (2.81)	0	17	11 (36.67)	5	1 (5.88)
Total	26 (43.33)	22 (36.67)	12 (20)	60	30 (50)	18 (30)	12 (20)

Statistical analysis for association of anxiety and duration of schizophrenia:  $\chi^2=9.851$ ,  $d(f)=2$ ,  $P=0.0072$ . Statistical analysis for association of anxiety and PANSS score predominant symptom:  $\chi^2=8.276$ ,  $d(f)=2$ ,  $P=0.015$ , PNAS: Positive and negative syndrome scale

**Table 4: Relation of co-morbid anxiety and QOL of patients suffering from schizophrenia**

Anxiety	WHO QOL-BREF					
	Q1	Q2	D1	D2	D3	D4
<b>Absent</b>						
Mean	3.19	2.80	20.38	17.51	7.7	19.83
SD	1.20	1.30	4.81	3.74	1.34	3.23
Minimum	1	1	12	13	6	16
Maximum	5	5	27	24	11	27
<b>Mild</b>						
Mean	3.67	3.33	23.33	19	8.33	23.67
SD	0.58	1.15	5.68	5.57	2.08	4.04
Minimum	2	1	17	13	6	19
Maximum	5	5	28	24	10	26
<b>Mild-moderate</b>						
Mean	2.67	2.78	18.55	16.22	7.22	20.77
SD	1.23	1.20	4.79	4.43	1.39	2.728
Minimum	2	1	10	10	5	17
Maximum	5	5	24	22	10	25
<b>Moderate-severe</b>						
Mean	2.12	2.41	17.11	15.70	7.11	18
SD	1.27	1.22	5.09	3.38	1.16	2.12
Minimum	1	1	10	10	5	15
Maximum	4	5	25	21	9	22
P value	0.02	0.6	0.011	0.05	0.3	0.009

QOL: Quality of life, SD: Standard deviation

**Table 5: Distribution of different type of anxiety disorders among patients of schizophrenia**

Anxiety disorders	Number of patients	Percentage
Social anxiety	9	31.03
Specific phobia	0	0
GAD	4	13.79
PTSD	3	10.34
Panic disorders	7	24.13
OCD	6	20.68
Total	29	100

OCD: Obsessive-compulsive disorder, GAD: Generalized anxiety disorder, PTSD: Posttraumatic stress disorder

treating anxiety disorders when present in patients with schizophrenia spectrum could contribute to achieve more positive outcomes.<sup>13,14</sup>

Clinical aspect of schizophrenia and prevalence of anxiety:

This study was supportive to many previous study results stating higher prevalence of anxiety in patients with schizophrenia. Among the patients, who were diagnosed as schizophrenia, we found 66.67% patients had at least one anxiety symptom.

This prevalence estimated was consistent with previous studies. In a study done by Huppert and Smith.<sup>15</sup> 62% patients had at least one anxiety disorder. Tibbo *et al.*<sup>16</sup> study done on 90 patients found 73% prevalence of anxiety disorder in schizophrenic patients.

We found that anxiety was more prevalent (57.5%) in paranoid patients than non-paranoid patients. The observed difference in prevalence was statistically significant. This finding was consistent with many other studies.<sup>15,17,18</sup>

Furthermore, we added more systematic evaluation of relation of severity of anxiety with subtypes of schizophrenia. Moderate to severe degree of anxiety was more (60.87%) prevalent in paranoid type of patients than nonparanoid (50%) type of patients. Comparison of severity of anxiety was to our knowledge is done in our study first time.

In this study, out of 29 patients with co-morbid anxiety 18 (62.06%) were of <2 years duration of schizophrenia. Our study suggest that presence of anxiety is more common associated with lesser duration (acute illness) of schizophrenia illness. The association we found was statistically strongly significant ( $P = 0.007 < 0.05$ ). No earlier study has included duration of schizophrenia as a variable in studying the relationship between schizophrenia and anxiety. The study of Achim *et al.*<sup>17</sup> have given relation of anxiety with first episode and non-first episode schizophrenia, where he found first episode present with high rate of anxiety.

The relation between anxiety and predominant symptom of schizophrenia (a/c PANSS scale) suggests that out of 29 schizophrenic patients with co-morbid anxiety, 20 (68.96%) had predominantly positive symptoms. This association was statistically significant ( $P = 0.015 < 0.05$ ). In a study conducted in Turkey, positive symptoms were higher in schizophrenic patients with panic symptoms.<sup>19</sup>

**Anxiety and QOL of patients with schizophrenia:**

Schizophrenia is a chronic condition with physical, psychological, emotional and cognitive deterioration. Anxiety and other co-morbidities further add to deterioration.

In this study, we co-related anxiety and its severity with QOL of patients with schizophrenia. We used WHO QOL-BREF QOL scale include six aspects of QOL.

- Q1- Self-perception about QOL
- Q2- Self-perception about general health
- Domain 1 - Physical health
- Domain 2 - Psychological health
- Domain 3 - Social relationship, and
- Domain 4 - Environment.

We found, lowest average score (i.e., poor QOL) for WHO QOL-BREF on self-perception of QOL ( $P = 0.02 < 0.05$ ).

Physical health (D<sub>1</sub>) was poorer in patients having moderate to severe co-morbid anxiety (mean = 17.11) as compared to those patients without anxiety (mean = 20.38).

Psychological health (D<sub>2</sub>) perception was also impaired significantly ( $P = 0.05$ ) in severe anxiety patients than other.

Environmental aspect (D<sub>4</sub>) of QOL also showed significant deterioration due to presence of anxiety. This difference was strongly significant ( $P = 0.009$ ) on statistical analysis.

This result was also replicated many times in previous studies. Dernovšek *et al.* study<sup>20</sup> estimated that anxiety symptoms have a significant negative impact on the QOL of patients with schizophrenia.

Relation of specific type of anxiety disorder with schizophrenia:

DSM-IV-TR based SCID-I-Clinician Version was used to confirm the diagnosis of anxiety disorders in patients who have co-morbid anxiety with schizophrenia. We found highest prevalence of social anxiety among of schizophrenic patients.

This finding was consistent with most of the earlier studies. Study of Achim *et al.*<sup>17</sup> have shown pooled prevalence rates of 14.9% (CI 8.1-21.8%) for social phobia, 12.1% (7.0-17.1%) for OCD, 10.9% (2.9-18.8%) for GAD, 9.8% (4.3-15.4%) for panic disorders, and 12.4% (4.0-20.8%) for PTSD.

We found rate of panic disorder as 24.13% and this rate of this study was also consistent with the studies conducted by Tibbo *et al.*,<sup>16</sup> and Braga *et al.*<sup>21</sup>

### Strengths and Limitations of Study

In our study, the size of sample was sufficient and was corresponding to earlier studies to calculate prevalence. However to calculate exact relationship of various anxiety disorders larger sample size will be needed.

In our study, we compared two new variables of schizophrenia namely type of schizophrenia and duration of schizophrenia, with degree of severity of co-morbid anxiety, which, to our knowledge, were never studied in any of the previous studies.

This study being cross-sectional in design, did not check on persistence of anxiety symptoms. Furthermore failing to apply scales for specific anxiety disorders caused deficiency in determining detailed characteristics of that disorder.

The effect and side effect of anti-psychotics and other medications have not been considered in this study.

## CONCLUSION

From the observations and discussion, it is clearly evident from this study that the patients with schizophrenia have high prevalence of anxiety.

Anxiety also leads to significant impairment of QOL of patients.

With proper screening and detailed evaluation, anxiety is required to be detected in early stages and treated, which can further improve the prognosis of schizophrenia.

These results emphasize the importance of determining anxiety symptoms and co-morbid anxiety disorders in the clinical diagnosis, prognosis and treatment of schizophrenia and propose new research in treatment approaches for the agenda. Thus, reducing the suffering and also improve the QOL of these patients.

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# Role of Oral Prophylaxis with the Use of Erich Arch Bars: A Randomized Controlled Trial

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## Abstract

**Introduction:** In the management of maxillofacial fractures intermaxillary fixation (IMF) is the basic and fundamental principle. Various commonly used techniques for IMF include arch bars and various dental wirings. The aim is to report gingival inflammatory changes after applying arch bars and reversal of inflammatory changes after removal of arch bars.

**Materials and Methods:** Patients were divided into two groups, Group A and Group B depending on the treatment plan indicated. In Group A, 50 patients were treated with closed reduction and IMF was kept for 4-6 weeks. In Group B, 50 patients treated with open reduction and internal fixation on Champy's line of osteosynthesis under general anesthesia and the arch bar was kept for 10 days. Half of the subjects of each group received the oral prophylaxis at the time of arch bar removal (Group A1 and Group B1). The patients were examined for injury to gums and cheek, avulsion of teeth and wire injuries to the operator and assistant including needle stick injuries, perforation of gloves, fetid odor, coated tongue, iatrogenic injury to adjacent teeth, orthodontic movement of teeth, ischemic necrosis of the periodontium and mucosa, oral hygiene index simplified, Papillary bleeding index, and Russel periodontal index.

**Results:** Orthodontic tooth movement, iatrogenic injury to adjacent teeth and ischemic necrosis of the periodontium and mucosa was reported with no statistical significant difference between groups and subgroups. There was a statistical significant difference in oral hygiene index-simplified, papillary bleeding index and Russel periodontal index between the patients in Group A1 and A2 and also between Group B1 and B2.

**Conclusion:** As per the observations of this study all the patients with arch bars suffer from gingival and periodontal injuries, so it is recommended that oral prophylaxis after removal of arch bar should always be done for early recovery of gingival and periodontal recovery.

**Key words:** Erich arch bar, Gingival inflammation, Maxillofacial injuries, Oral prophylaxis

## INTRODUCTION

The principles of management of fractures of hard tissues are reduction, fixation, and immobilization of the bony fragments. Mandibular fractures can be treated by closed reduction (intermaxillary fixation [IMF]) and open reduction (osteosynthesis with or without IMF). IMF can be achieved by eyelets, arch bars, and glimmers wiring,

etc. Arch bars have been used widely for management of maxillomandibular injuries since World War 1.<sup>1,2</sup> Carl<sup>3</sup> in Germany and Gilmer<sup>4</sup> in the United States used ordinary round bar which was ligated to teeth with bass ligation wires. Blair and Ivy<sup>5</sup> modified and flattened one side about 2 mm in width for better adaptation to dental arches for greater stability, little has changed since the introduction of arch bars. Application of arch bars with circumferential wiring is the most preferred method for IMF. Wire is passed around the teeth for fixation of arch bars. This causes gingival and periodontal injuries, difficulty in maintaining the oral hygiene, threat to percutaneous injury to operator or assistant by wire ends, mucosal ulcerations orthodontic movement of anterior teeth if not adapted properly, high chances of serological transfer of pathogens like hepatitis

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B virus, hepatitis C virus, and HIV.<sup>6,7</sup> The introduction of bone plating has reduced the prolonged periods of IMF. However, there is need of temporary IMF intraoperatively to assist reduction of fracture with teeth in occlusion and post-operatively to correct minor occlusal discrepancies. So, we decided to conduct a study at our tertiary care institute to note the incidences of iatrogenic injuries and complications/problem associated with the Erich arch bar and to evaluate the need of oral prophylaxis after the arch bar removal.

## MATERIALS AND METHODS

The study group consisted of 100 patients of trauma with history of RTA, fall, violence, etc., having fracture mandible and dentoalveolar region who reported to the Department of Oral and Maxillofacial Surgery, Indira Gandhi Government Dental College, Jammu and required IMF as part of treatment plan. After taking informed consent, clinical and radiographic examination of the patients was done and treatment plan formulated. Patients were divided into two groups, Group A and Group B depending on the treatment plan indicated. In Group A, 50 patients were treated with closed reduction and IMF was kept for 4-6 weeks. In Group B, 50 patients treated with Open Reduction and Internal Fixation on Champy's line of osteosynthesis under general anesthesia, and arch bar was kept for 10 days. Randomly, half of the subjects of both the groups received the oral prophylaxis at the time of arch bar removal (Group A1 and Group B1) while in the other half no oral prophylaxis was advised (Group A2 and Group B2). The Erich Arch bars were placed using circumdental wiring and removed by a single team of operator and assistant who were blinded of the groups (Figure 1). The patients were examined for injury to gums and cheek, avulsion of teeth during arch bar placement and wire injuries to the operator and assistant including needle stick injuries, perforation of gloves at the time of arch bar placement. On the day of arch bar removal fetid odor, coated tongue, iatrogenic injury to adjacent teeth, orthodontic movement of teeth, ischemic necrosis of the periodontium and mucosa, wire injuries to the operator and assistant were noted (Figures 2 and 3). Oral hygiene index simplified (OHI-S),<sup>8</sup> papillary bleeding index<sup>9</sup> and Russel periodontal index<sup>10,11</sup> was evaluated on 15<sup>th</sup> day, post arch bar removal (Figure 4).

## RESULTS

Of the 100 patients treated 82 were males and road traffic accidents was the most common cause of fractures. The mean age of the patients was 29.2 years, and the most common fracture site was parasymphysis followed by



Figure 1: Erich arch bar placement



Figure 2: Gingival laceration after arch bar removal



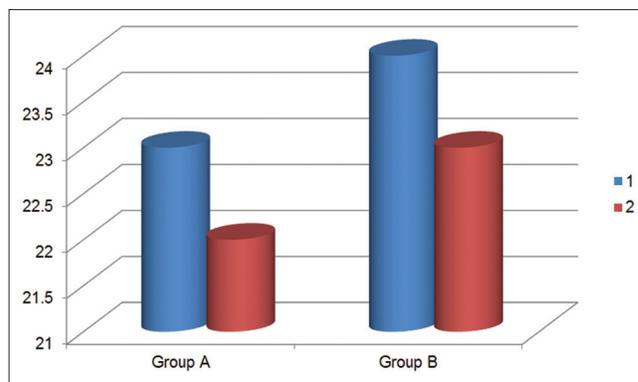
Figure 3: Periodontal inflammation after arch bar removal



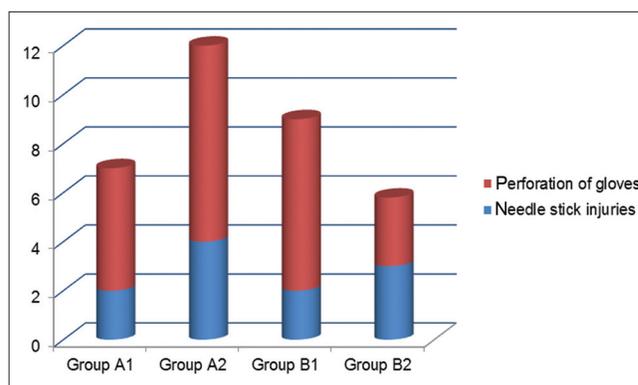
Figure 4: 15<sup>th</sup> day after arch bar removal

angle and condyle. There was no statistical significant difference in both the groups and subgroups based on

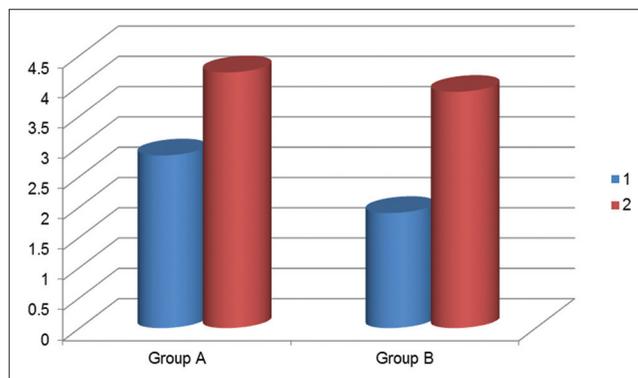
age, gender, etiology or site of the fracture. Almost all the patients in both group and subgroups had injuries to gums and cheeks during the arch bar placement (Table 1 and Graph 1). One patient in Group A1 had an avulsion of teeth which was implanted back into the socket and after 3 months Root canal treatment was done. The needle stick injury to operator and/or assistant was reported in 2 patients in Group A1, 4 patients in Group A2, 2 patients in Group B1 and 3 patients in Group B2 (Table 2 and Graph 2). The glove perforation of operator and/or assistant was reported in the remaining patients during arch bar placement. No needle stick injury was reported during arch bar removal. 100% of the patients in Group A1 and A2, and 92% in Group B1, and 96% in Group B2 reported coated tongue. The halitosis was reported 80% and 82% in Group A1 and A2, respectively, and 72% and 64% in Group B1 and B2, respectively (Table 3 and Graphs 3-5). Orthodontic tooth movement, iatrogenic injury to adjacent teeth and Ischemic necrosis of the periodontium and mucosa was also reported with no statistical significant difference between groups and subgroups. There was a statistical significant difference in OHI-S, papillary bleeding index and Russel periodontal index between the patients in Group A1 and A2 and also between Group B1 and B2. The patients whose oral prophylaxis were done at the time of arch bar removal reported better OHI-S, papillary bleeding index, and periodontal index in both Group A and Group B.



Graph 1: Injury to gums and cheek



Graph 2: Needle stick injury to operator and/or operator, perforation of gloves



Graph 3: Oral hygiene index - simplified

Table 1: Arch bar placement

Injury to gums and cheeks	Avulsion of teeth	Wire injuries to the operator and assistant, perforation of gloves
Group A		
1		
23	1	7
2		
22	0	12
Group B		
1		
24	0	9
2		
23	0	8

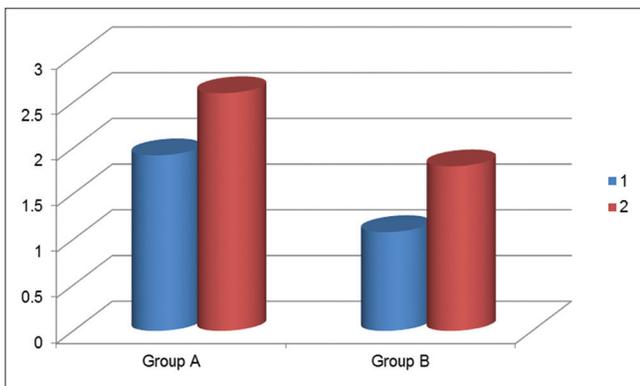
Table 2: Day of arch bar removal

Fetid odor	Coated tongue	Iatrogenic injury to adjacent teeth	Orthodontic movement of teeth	Ischemic necrosis of the periodontium and mucosa	Wire injuries, perforation of gloves
Group A					
1					
20	25	3	3	2	3
2					
21	25	1	2	3	0
Group B					
1					
18	23	0	1	1	1
2					
16	24	1	0	3	1

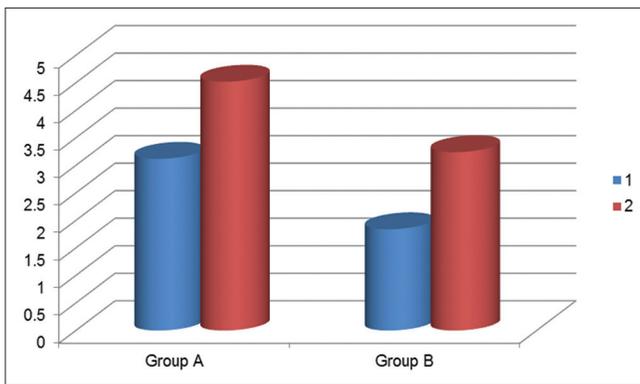
**Table 3: 15 days post arch bar removal**

Oral hygiene - OHI-S	Gingival bleeding - papillary bleeding index	Gingival inflammation and periodontal disease - periodontal index (Russel)
Group A		
1 71.25/25=2.85	48/25=1.92	78/25=3.12
2 105.5/25=4.22	65/25=2.6	113/25=4.52
Group B		
1 47.5/25=1.9	27/25=1.08	46/25=1.84
2 97.5/25=3.9	45/25=1.8	81/25=3.24

OHI-S: Oral hygiene index simplified



**Graph 4: Papillary bleeding index**



**Graph 5: Russel periodontal index**

## DISCUSSION

The management of maxillofacial injuries remains one of the most demanding and rewarding aspect of surgery because the patients with maxillofacial injuries not only suffer from physical agony but slight disfigurement can become an emotional distress for his whole life.<sup>1</sup> The main goals in successfully treating mandibular fractures include reduction, fixation and immobilization and achieving proper dental occlusion. It is also important to use techniques that reduce the percutaneous transmission

of blood-borne diseases, maintain proper oral hygiene in order to reduce gingival and periodontal diseases, prevent injuries to adjacent and supporting structures, reduce operating time, and hospital costs.<sup>2,12,13</sup> The treatment of maxillofacial fractures involve different methods from bandages and splinting to methods of open reduction and internal fixation, requiring control of the dental occlusion with the help of IMF with the traditional methods.<sup>2</sup> Various methods have been used for IMF in the management of mandibular fractures. The most common technique is to use eyelets or arch bars. The Erich arch bars have been used mainstay in management of maxilla mandibular fractures since World War 1.<sup>1</sup>

The most common and trusted method for mandibular fracture is the application of Erich arch bar for IMF with the help of circumdental wiring, yet circumdental wiring has its own shortcomings. Nevertheless, it has following disadvantages: wires have to pass below the gingival margin to guarantee stability, chances of gingival injury are more and compromises the health of periodontium, rounded wire edges collects food debris and causes gingival inflammation and difficulty in maintaining oral hygiene result in fetid breath.<sup>1</sup>

Most of our patient had injuries to gums and cheeks during the arch bar placement. During arch bar placement, optimum tension, and stable placement is a difficult task, breakage of wires during and after placement of wire is not uncommon which encounter instability of appliances. Passing of dental wires in patient with reduced mouth opening was also difficult. While passing of the wires and manipulating the fracture fragments, there was incidences of accidental pricking of the wire end to the hands of the operator or the assistant, and perforation of gloves. The most common site for perforation of gloves is the non-dominant hand. The similar finding were also reported in other studies.<sup>14,15</sup> The rounded wire edges collected food debris and caused gingival inflammation and there was difficulty in maintaining oral hygiene which result in fetid breath and coated tongue. Few patients also reported the orthodontic tooth movement. The ill-fitting of Erich arch bar and over tightening of wires caused orthodontic movement of anterior teeth. Ischemic necrosis of the periodontium and mucosa and injury to adjacent teeth was possibly caused by the tension of the wire and the pressure inserted on the gums. There was also an avulsion of tooth because of application of inadvertently excessive force on the mobile tooth. Recent studies have reported needle-stick injuries, the high plaque index, periodontal damage, and movement of the teeth in lateral and extrusive direction.<sup>2,16-20</sup>

In our study, the patients in who oral prophylaxis was advised after the arch bar placement reported better oral

hygiene. The patients reported better scores of OHI-S, papillary bleeding index and Russel periodontal index in both Group A and Group B in which oral prophylaxis have been performed. No previous study has evaluated the oral hygiene and periodontal health indices with Erich arch bar placement and the role of use of oral prophylaxis in improving the oral hygiene of the patient. During the period of IMF, there was difficulty in maintaining the oral hygiene, which resulted in coated tongue, fetid odor, calculus and debris deposition which has detrimental effect on the periodontium. The oral prophylaxis at the time arch bar removal of seems to reverse or reduce these effects. However, we did not evaluate the pre-operative OHI-S, periodontal index or papillary bleeding index, the damage to periodontium/degradation of oral health with the placement of Erich arch bar could not be assessed.

## CONCLUSION

As per the observations of this study all the patients with arch bars suffer from gingival and periodontal injuries, so it is recommended that oral prophylaxis after removal of arch bar should always be done for early recovery of gingival and periodontal recovery. However, further studies are required in which pre-operative evaluation and their comparison with final periodontal health can be made to correctly assess the periodontal damage with the arch bar placement.

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# Role of Penile Color Doppler in the Evaluation of Erectile Dysfunction

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## Abstract

**Background:** Color duplex Doppler is a non-invasive tool of evaluation of the vascular mechanism of erectile dysfunction (ED). It can be used to determine the integrity of the vascular mechanism and to differentiate between arterial and venous insufficiency.

**Materials and Methods:** An observational study was conducted at the Department of Radiology Vydehi Medical College and Research Center from June 05, 2013 to September 02, 2015. A total of 33 consecutive patients presenting with symptoms of ED and undergoing penile color Doppler evaluation with the injection of 2 ml of papaverine were included in this prospective study.

**Results:** The baseline diameter of the vessels at pre-injection was <1 mm in 46% of the patients, the majority of the patients 52% showed a baseline diameter of 1-1.5 mm. Post-injection of papaverine the peak increase in the diameter of the vessels in 43% of the patients showed an increase of <1.5 mm. However, 52% of the patients showed an increase between 1.5 and 2.5 mm. The average peak diameter was 1.71 mm and the  $P < 0.001$ , which was significant. 46% patients with low peak systolic velocity (PSV) values (<25 cm/s) in the cavernosal artery were considered to have arterial insufficiency, 9% (3) of the patients had an end-diastolic velocity of >5 cm/s had normal arterial function, that is, normal PSV. Adequate arterial inflow, a short duration erection, with the persistent antegrade flow of >5 cm/s throughout all phases suggestive of venous leak. 42% of the patients studied were found to be functional where no cause could be ascertained.

**Conclusion:** When arterial insufficiency is found, patients can be considered to have systemic arteriovascular disease. On the other hand, veno-occlusive dysfunction is not correlated with systemic arterial vascular problems. In conclusion, investigating of ED by color duplex Doppler is not time-consuming and may help establish an accurate diagnosis of vascular causes of impotence.

**Key words:** Color, Doppler, Erectile dysfunction, Papaverine, Ultrasonography

## INTRODUCTION

Erectile dysfunction (ED) is a common health problem which affects men of various age groups; it affects both young and middle-aged men. Color duplex Doppler is a non-invasive tool of evaluation of the vascular mechanism of ED which can result from psychogenic, endocrinologic, neurogenic, pharmacologic, and vasogenic causes. Color duplex Doppler can be used to determine the integrity

of the vascular mechanism and to differentiate between arterial and venous insufficiency.

Penile erection is a complex phenomenon, which includes coordinated interaction of the arterial, venous sinusoidal and nervous systems. The penile erectile tissue, specifically the cavernous smooth musculature and the smooth muscles of the arteriolar and arterial walls, plays a key role in the erectile process.<sup>1</sup> A defect or incoordination in any of these systems may result in ED. ED is defined as the consistent inability to generate or maintain an erection of sufficient rigidity for sexual intercourse. Around 10% of men aged 40-70 years have complete, 17.1% have mild, and 25.2% have moderate amount of ED.<sup>2</sup>

ED is closely linked to the general state of both physical and psychological wellness. Among the major risk

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factors are heart disease, arterial hypertension, diabetes, hyperlipidemia, as well as sedentary lifestyle, smoking and alcohol abuse.<sup>3</sup> Sexual dysfunction is common in patients with alcohol dependence. Heavy drinking proportionately increases the risk.<sup>4</sup>

The normal chain of events leading to penile erection begins with psychological factors that lead to transmission of parasympathetic impulses to the penis. The walls of the sinusoids and arterioles of the corpora cavernosa relax, which leads to an increased inflow of blood via the cavernosal artery. With filling of the sinusoidal spaces, corporal veno-occlusive mechanism works. The emissary veins exiting the corpora are passively compressed against the fibrous tunica albuginea following which rigid penile erection is achieved and maintained. Detumescence occurs due to contraction of trabecular smooth muscle in the corpora cavernosa after neurological stimulation.<sup>2,3</sup>

ED is caused by the interruption in the chain of events including psychogenic, neurogenic, arteriogenic, and venogenic causes. Often more than one cause is combined. Establishing a specific cause is important particularly in young men because of the frequency of correctable vascular abnormalities. Pure arteriogenic impotence accounts for about 30% of cases, and isolated venogenic impotence is found in about 15%. Often ED is caused by a combination of arteriogenic and venogenic causes. Occasionally, organic impotence is caused by morphological abnormalities of the penis such as peyronies disease (PD).<sup>5</sup>

Organic etiologies include vascular, neurogenic, PD, medication side effects and endocrinologic sources. Vascular causes are commonly due to focal arterial occlusive disease.<sup>6</sup>

The cavernosal arteries are the primary source of blood flow to the corpora cavernosa; the dorsal arteries supply blood to the skin and glans of the penis. The cavernosal arteries are connected by multiple anastomotic channels to the dorsal arteries. Arteriography with selective internal iliac angiography is considered the gold standard in the evaluation of arteriogenic impotence. However, this technique is invasive and therefore not suitable as a screening examination.<sup>5</sup> The use of Doppler ultrasound in the assessment of the penile vasculature was first described in 1985.<sup>7</sup>

Penile color Doppler sonography is a valuable method for evaluating ED and it has become the first line diagnostic tool in diagnosing vasculogenic impotence.<sup>8</sup> This method requires intracorporeal injection of a vasoactive substance such as papaverine hydrochloride or prostaglandin E1, however, there are some concerns about the safety of

this method due to the intracorporeal pharmacological injection, which may cause priapism as a complication, histological changes and functional impairment resulting in penile fibrosis.<sup>9</sup>

In 1982 during a vascular reconstructive procedure, Ronald Virag noted that an infusion of papaverine into the hypogastric artery produced an erection. In 1983, a dramatic demonstration of the efficacy of penile self-injection was offered by Brindley, who injected himself.<sup>10,11</sup> Virag *et al.* showed that precise Doppler sampling and blood velocity measurements of the deep cavernosal arteries could be performed before and after intracavernosal injection of vasodilating agents and 75% increase in vessel diameter is good indication of normal arterial flow into the cavernosal artery.<sup>5,12</sup>

Commonly many investigators use 2 ml solution of 60 mg of papaverine into either the right or left corpus cavernosum.<sup>13,14</sup> The investigators concluded that a peak systolic velocity (PSV) of >25 cm/s was normal.<sup>5,15,16</sup> The parameters that indicate the presence of arterial disease are a subnormal response to vasoactive agents, a diameter of <60% increase in the cavernosal artery, and a PSV of the cavernosal arteries <25 cm/s. In the presence of normal arterial function, Doppler findings suggestive of an abnormal venous leak are persistent end-diastolic velocity (EDV) of the cavernosal artery >5 cm/s and demonstration of flow in the deep dorsal vein. The development of Diastolic flow reversal after an injection has been found to be a reliable indicator of venous competence.<sup>5</sup>

## MATERIALS AND METHODS

An observational study was conducted at the Department of Radiology, Vydehi medical college and research center from July 05, 2013 to September 02, 2015. Informed consent was obtained from all patients prior to participation. A total of 33 consecutive patients presenting with symptoms of ED and undergoing penile color Doppler evaluation with the injection of 2 ml of papaverine were included in this prospective study.

### Exclusion Criteria

Patients with heart diseases, known case of PD and patients with history of drug allergy were excluded from the study.

A gray scale ultrasound was performed in transverse and the longitudinal sections to see any plaque or any other abnormality. A brief history of the patient was taken with adequate privacy and in a quiet environment to allay patient anxiety as much as possible. The study was performed

by one of two experienced radiologists. All studies were performed on a Philips HD7 ultrasound machine with L12-3 broadband linear array high-frequency transducer (12-13 MHz frequency range) was used. Doppler was performed with the patient supine and the penis in the anatomical position, lying on the anterior abdominal wall. The following protocol for penile Doppler US was followed. Factors such as accurate gate placement, sampling and angle correction were optimized for consistent and reproducible results. Cavernosal artery spectral waveform was measured at the base of the penis as angle correction is optimal, and the velocities are highest here.

Intracavernosal injection of 2 ml of papaverine with a 28 G needle under ultrasound guidance and aseptic precautions close to the base of the penis was done and massaged in. The peak systolic and EDV measurements were obtained in the right cavernosal artery at 5 min intervals for a total of 30 min. The systolic velocity of <25 cm/s was used as the threshold for arterial insufficiency. An EDV of >5 cm/s was used to predict venous incompetence (Figures 1,2). Erection was graded at a 10 min as follows: 1 - no erection; 2 - slight tumescence; 3 - full volume without rigidity; 4 - incomplete rigidity but sufficient for sexual intercourse; and 5 - full erection with unbending rigidity.<sup>10,17</sup>

## RESULT AND DISCUSSION

An observational study was carried out at the Department of Radiology in Vydehi Institute of Medical Sciences and Research Centre, Bengaluru, Karnataka, India. The statistical analysis was carried out using the IBM SPSS version 22 (SPSS Inc., Armonk, NY, USA).

In this study, the 23 patients (69.7%) were referred for penile Doppler investigation from the Department of Urology - U, 7 (21.2%) patients from Department of Psychiatry – Pand, 3 (9.1%) patients from the Department of General Medicine - M respectively (Graph 1). The age distribution of the patients studied was from 18 to 58 years, majority of the patients studied were in the 3<sup>rd</sup> decade (Graph 2). 23 (70%) patients out of a total of 33 patients were married (Graph 3). Age distribution of patients studied (Table 1).

Personal habits of 33 patients studied showed a significant 73% of the patients were smokers (Graph 4), a study by Austoni *et al.* showed a dose - and duration-response relationship between smoking and erectile dysfunction.<sup>18</sup> Another population-based cross-sectional study of 1580 participants study by Chew *et al.* compared non-smokers, former smokers and smoker and found smokers to have significantly higher odds of ED.<sup>19</sup> A study by Wu *et al.* of 2686 Chinese men revealed smokers who smoked  $\geq 20$

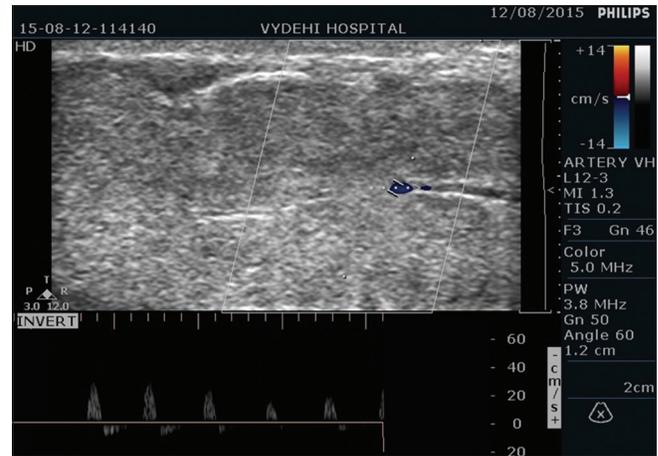


Figure 1: Normal peak systolic velocity of >35 cm/s with end diastolic flow reversal, suggesting normal study

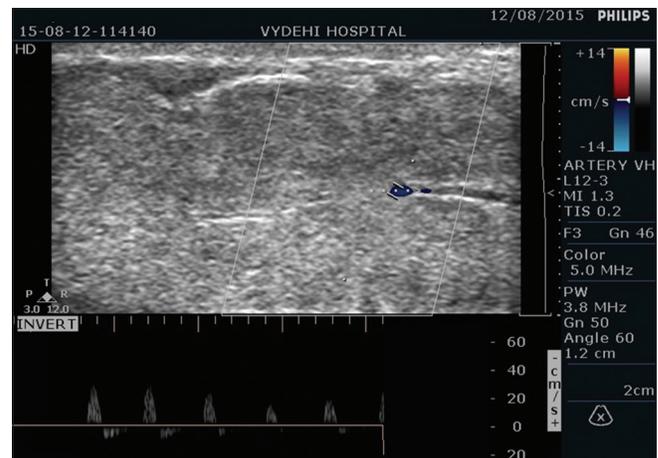
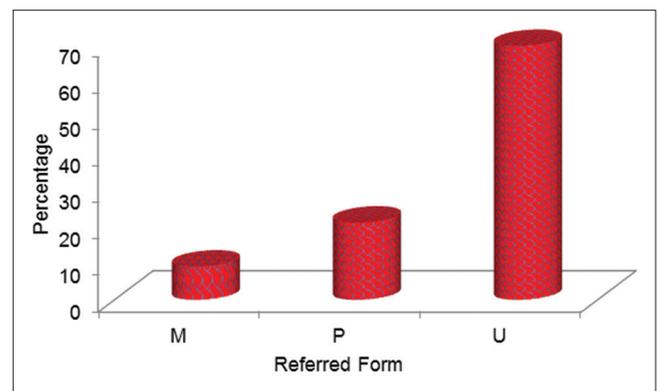
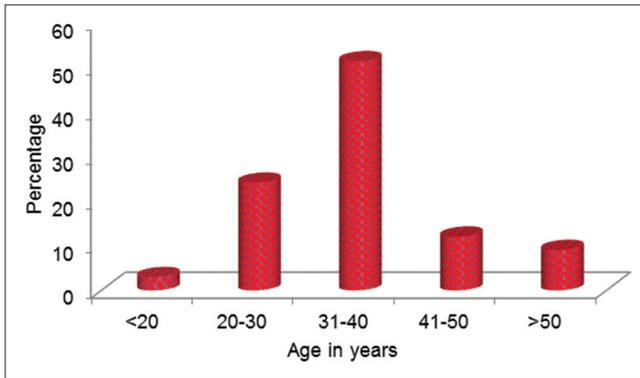


Figure 2: Normal peak systolic velocity of >35 cm/s with end diastolic flow reversal, suggesting normal study

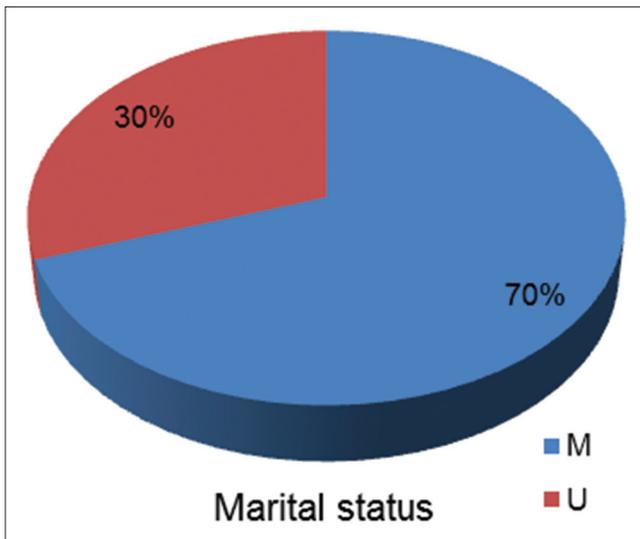


Graph 1: Patients referred from various dept.'s

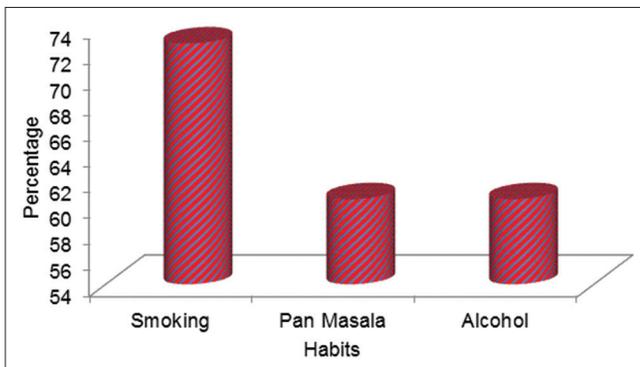
cigarettes daily had a significantly increased risk of ED than never smokers the study also revealed heavy smoking might cause ED and that the duration of the habit increases the risk of ED.<sup>20</sup> Furthermore, our study highlights the potential interaction of smoking with ED.



Graph 2: Age distribution of patients studied



Graph 3: Marital status of patients studied



Graph 4: Personal habits of patients studied

Table 1: Age distribution of patients studied

Age in years	Number of patients	Percentage
<20	1	3.0
20-30	8	24.2
31-40	17	51.5
41-50	4	12.1
>50	3	9.1
Total	33	100.0

Mean±SD: 36.12±8.41, SD: Standard deviation

A significant 61% of patients were found to have a history of alcohol intake. A study by Dachille *et al.* demonstrated a significant relationship between alcohol consumption and ED (Table 2).

60% of the patients had a history of consumption of pan masala, a recent animal experimental study by Nigam and Venkatakrishna-Bhatt on the effect of blended tobacco products on the reproductive system of mice showed a significant adverse effects on the reproductive system.<sup>21</sup> There are no studies on humans correlating consumption of pan masala with ED. In the present study, we found majority of patients who were addicted to pan masala developed ED in due course of time.

Only 6 (19%) patients had a history of hypertension, none of the patients studied had a history of diabetes mellitus. In the second Princeton consensus, Jackson *et al.* concluded that a man with ED and no cardiac symptoms is a patient with cardiac (or vascular) disease until proven otherwise.<sup>22</sup>

The base-line diameter of the vessels at 0 min post-injection was <1 mm in 46% of the patients studied, the majority of the patients 52% showed a baseline diameter of 1-1.5 mm. One patient had a baseline diameter of more than 1.5 mm. Post-injection of paperavine the peak increase in the diameter of the vessels in 43% of the patients showed an increase of <1.5 mm. However, 52% of the patients showed an increase between 1.5 and 2.5 mm. Two patients showed an increase more than 2.5 mm (Table 3). The average peak diameter was 1.71 mm and the  $P < 0.001$  which was significant (Table 4). A study by

Table 2: Relationship between alcohol consumption and ED

	Number of patients (n=33)	Percentage
Smoking	24	72.7
Pan masala	20	60.6
Alcohol	20	60.6

Table 3: The base-line diameter of the vessels immediately after injection of paperavine

	Number of patients (n=33)	Percentage
Base line diameter of vessel (mm)		
<1	15	45.5
1-1.5	17	51.5
>1.5	1	3.0
Increase in diameter after injection (mm)		
<1.5	14	42.4
1.5-2.5	17	51.5
>2.5	2	6.1

Base line diameter of vessel (mm)/increase in diameter after injection (mm)

Acharya and Vasu showed the post-injection mean diameter was 1.0 mm,<sup>23</sup> however, our study found a mean increase of 1.7 mm (Graph 4).

In our study, the PSV was graded as Grade I: <25 cm/s, Grade II: 25-30 cm/s, and Grade III: >30 cm/s. The EDV was graded as <5.0 cm/s and above >5.0 cm/s (Table 5). In our study, we used the PSV as the reference standard to diagnose arteriogenic impotence. In our study, 46% patients with low PSV values (<25 cm/s) in the cavernosal artery were considered to have arterial insufficiency (Figures 3-10). We found that reversal of flow in is a clue to the diagnosis of arteriogenic impotence. However, in case of patients with PSV values of more than 30 cm/s, this finding contributed little to the diagnosis of arteriogenic impotence (Table 6).

In men with veno-occlusive disorder, the usual criterion for diagnosing veno-occlusive dysfunction has been an EDV >5 cm/s.<sup>16,23</sup> Again, various threshold EDV values have been suggested between 5 and 7 cm/s as diagnostic of venous incompetence.<sup>24-26</sup> However, such threshold values for EDV can be misleading if arterial insufficiency is present. This observation was not confirmed in all studies, and there is a poor correlation of color Doppler ultrasound findings and veno-occlusive dysfunction when diagnosis was made. In our study, 9% (3) of the patients had an EDV of >5 cm/s had a normal arterial function, that is,

**Table 4: Peak increase in the diameter of the vessels post-injection of papaverine**

Variables	Baseline	After injection	Difference	t value	P value
Diameter of vessel (mm)	1.05±0.33	1.71±0.55	0.65	11.033	<0.001**

Base line diameter of vessel (mm)/increase in diameter after injection (mm), \*\* P<0.01

**Table 5: Grading of PSV**

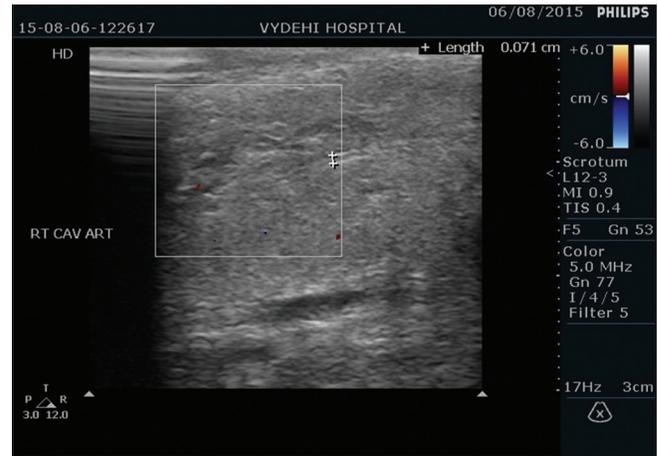
	Number of patients (n=33)	Percentage
Max PSV cm/s		
<25	15	45.5
25-30	1	3.1
>30	17	51.5
Max EDV cm/s		
<5.0	30	90.9
>5.0	3	9.1

Max PSV cm/s, Max EDV cm/s, PSV: Peak systolic velocity, EDV: End-diastolic velocity

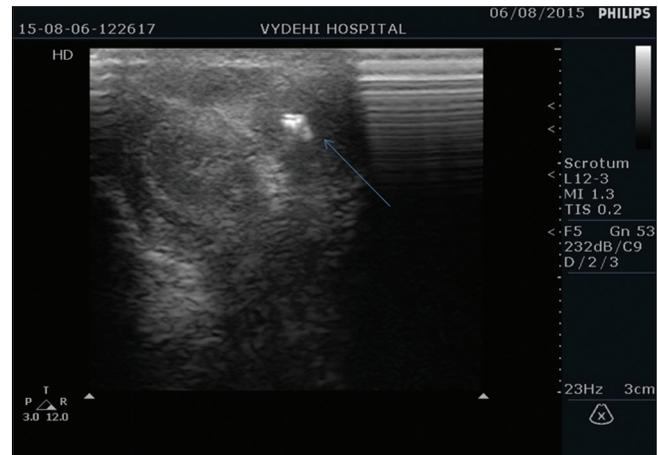
**Table 6: Total cases of arterial insufficiency and venous insufficiency**

Insufficiency	Number of patients (n=33)	Percentage
Arterial insufficiency	16	48.5
Venous insufficiency	2	6.1

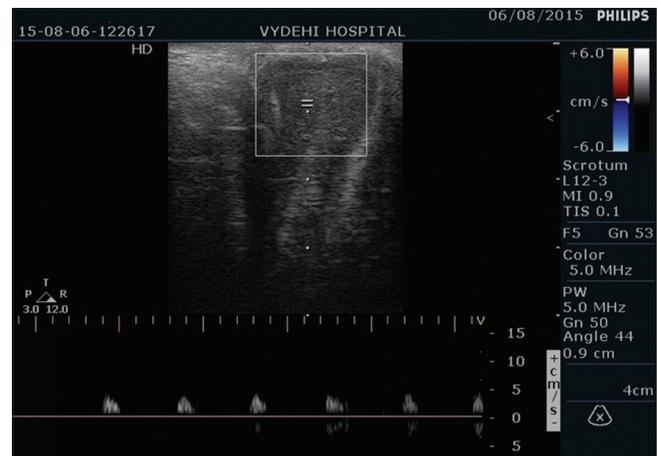
normal PSV (Graph 9). Adequate arterial inflow, a short duration erection, with the persistent antegrade flow of >5



**Figure 3: Pre-injection calipers showing the baseline diameter of vessels**



**Figure 4: Arrow showing the intracavernosal injection of papaverine**



**Figure 5: Doppler evaluation in demumiscnt srstage showing monophasic waves with low peak systolic velocity of <5 cm/s.**

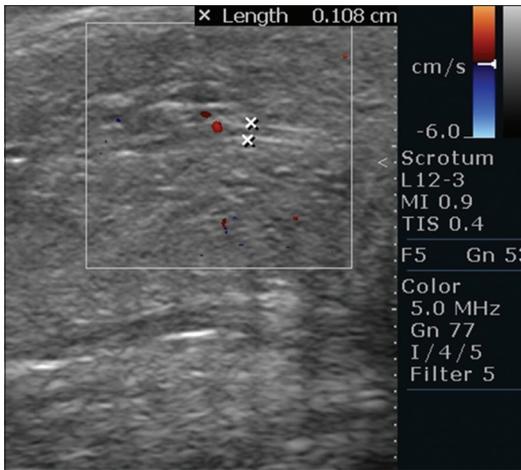


Figure 6: Post-intracavernosal injection of papaverine, calipers revealing increase in diameter of intracavernosal vessel

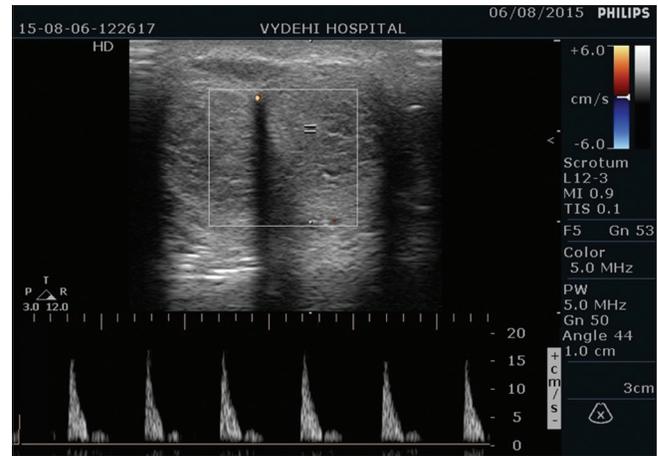


Figure 9: 15 m post-injection showing low peak systolic velocity of 15 cm/s with diastolic flow of <5 cm/s

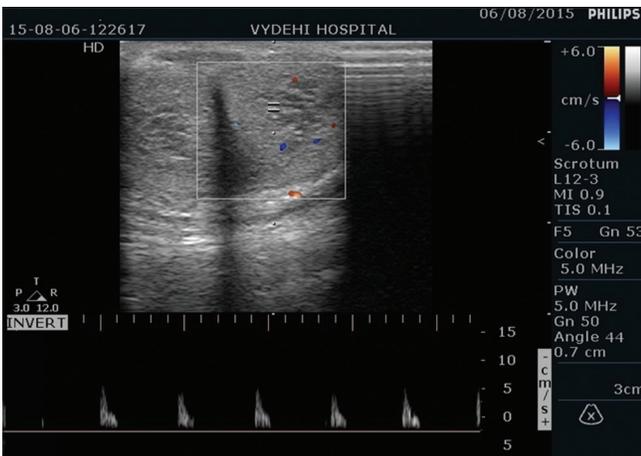


Figure 7: Post-injection showing monophasic waves with low peak systolic velocity of 5 cm/s with minimal diastolic flow



Figure 10: 25 M post-injection showing low peak systolic velocity of 15 cm/s with diastolic flow reversal. Interpretation: This patient the study revealed no significant increase in the diameter of cavernosal vessel following papaverine injection and following papaverine injection the maximum peak systolic velocity remained <15 cm/s with diastolic flow reversal, suggesting arterial insufficiency

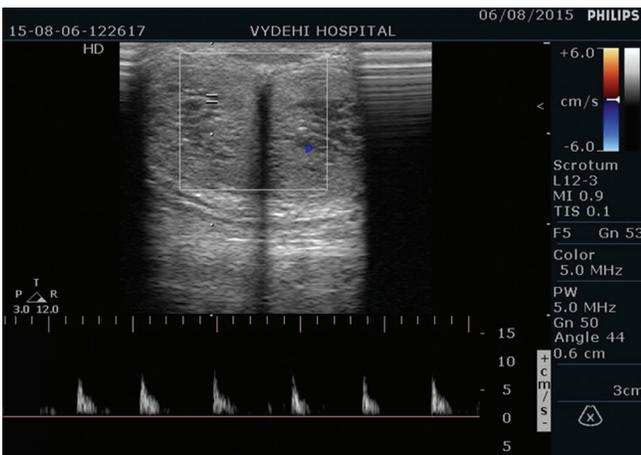
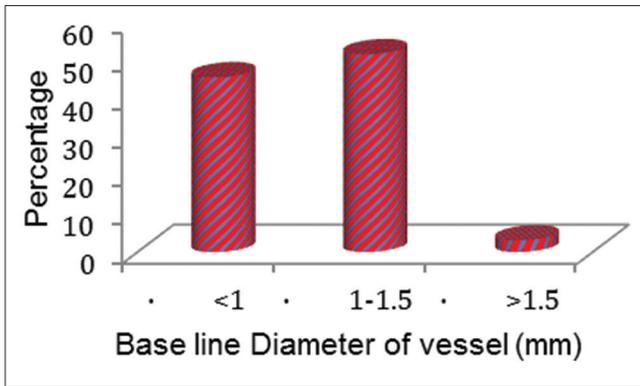


Figure 8: 10 m post-injection showing low peak systolic velocity of 10 cm/s with diastolic flow of <5 cm/s

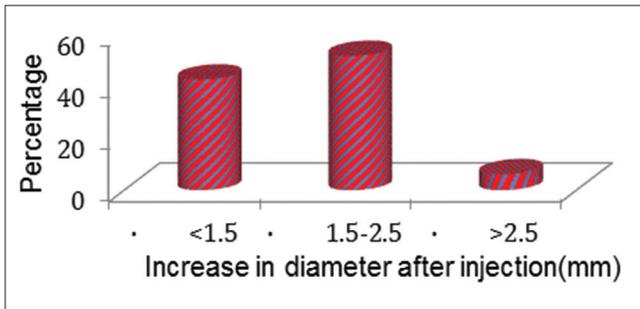


Figure 11: Baseline arrows indicating right and left corpus cavernosa

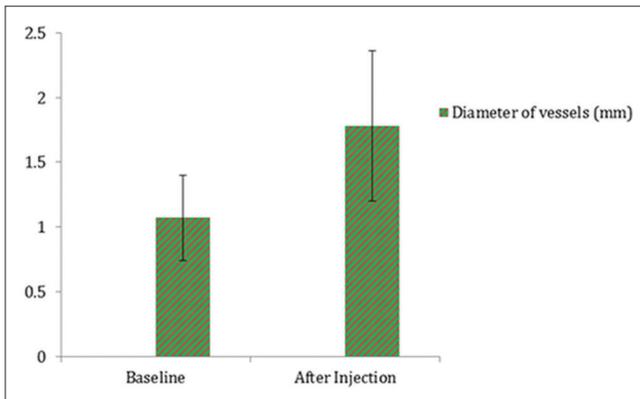
cm/s (angle corrected) throughout all phases suggestive of venous leak (Figures 11-19). In 42% of the patients studied



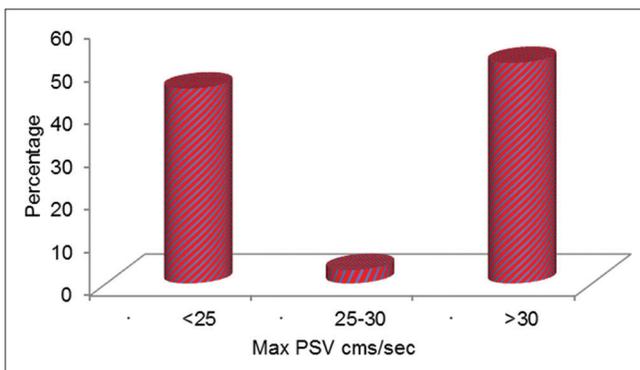
Graph 5: Percentage increase in diameter of the cavernosal arteries after injection of papaverine



Graph 6: Pre-injection baseline diameter of the cavernosal arteries studied



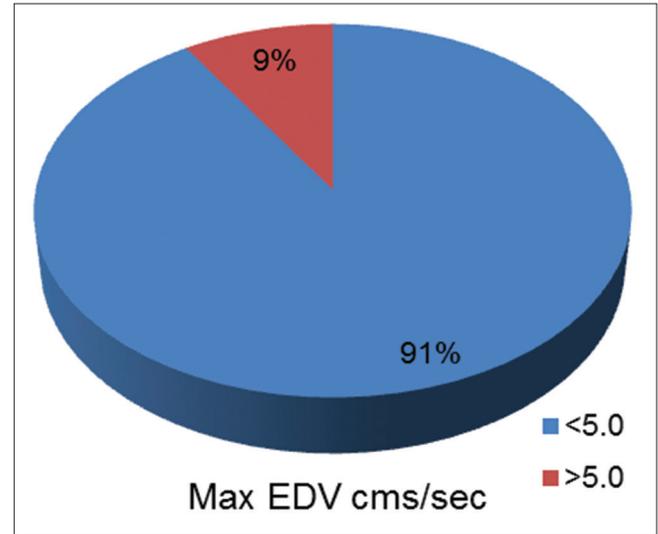
Graph 7: Base line diameter of cavernosal arteries before and after injection of papaverine



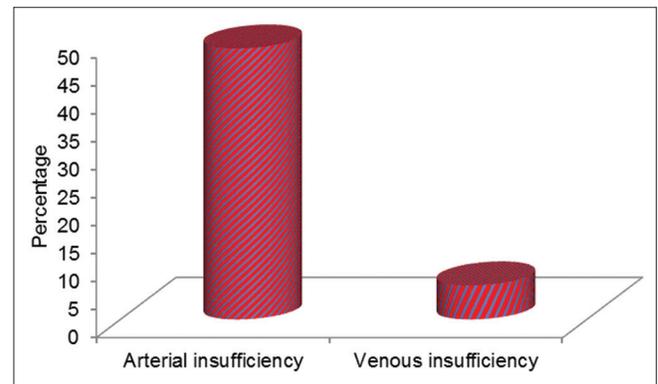
Graph 8: Percentage of Max PSV recorded

the vasculogenic cause could not be identified and were found to be functional (Graphs 5-8,10,11) (Table 7).

Base line diameter of the vessel at the time of injection was  $1.05 \pm 0.33$  mm with an increase in diameter after injection to  $1.71 \pm 0.55$  mm, The *P* value obtained was  $<0.001$  which was statically significant.



Graph 9: Percentage of patients with venous insufficiency



Graph 10: Percentage of patients with arterial and venous insufficiency

Table 7: Number of patients with functional insufficiency

Functional	Number of patients	Percentage
Nil	19	57.6
Yes	14	42.4
Total	33	100.0

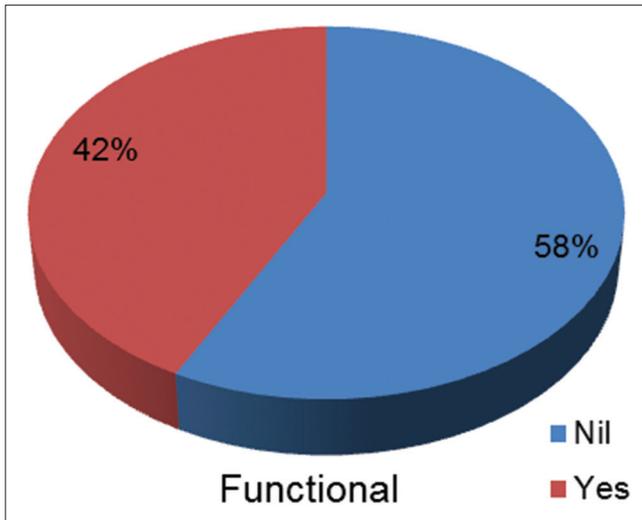
Table 8: Number of patients with complications

Complications	Number of patients	Percentage
Nil	31	93.9
Priapism	2	6.1
Total	33	100.0

45% (15) of the patients had a Max PSV <25 cm/s were considered to have arterial insufficiency (Graph 10),

52% (17) of the patients had a Max PSV >30 cm/s were considered normal (Graph 11).

Complication of priapism was found in 2 patients (Table 8). 18% of the patients studied had hypertension, 30 out of 33 patients had a history of mixed diet.



Graph 11: Percentage of patients with functional and vasculogenic causes of ED



Figure 14: 5 min post-injection



Figure 12: After injection arrow indicating intracavernosal injection of papaverine

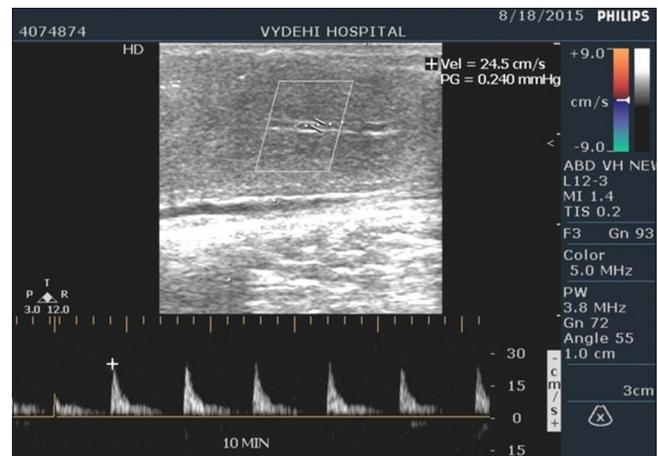


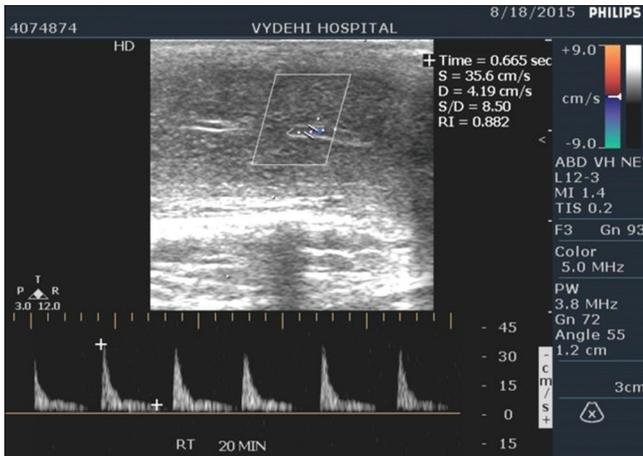
Figure 15: 10 min post-injection



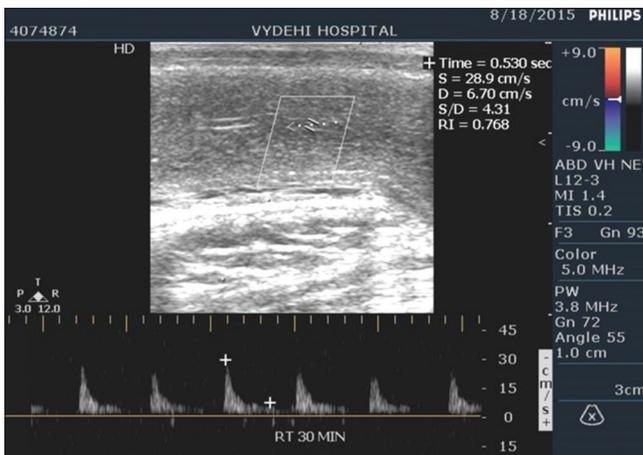
Figure 13: After injection, the calipers showing increase in diameter of cavernosal artery



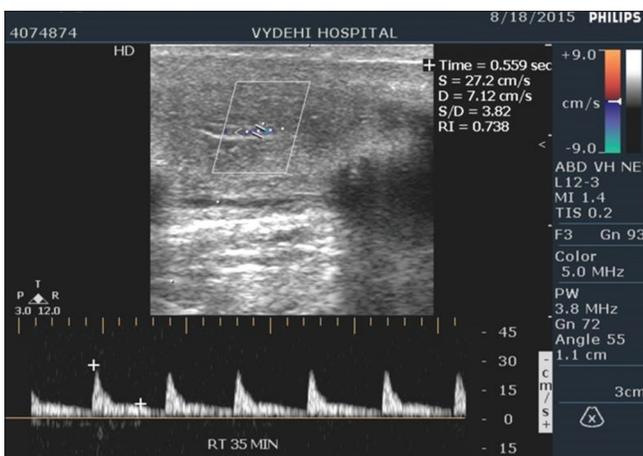
Figure 16: 15 min post-injection



**Figure 17: 20 min post-injection normal peak systolic velocity >35 cm/s is with continuous diastolic flow of >5 cm/s with no diastolic reversal**



**Figure 18: 30 min. Reduced peak systolic velocity with continuous diastolic flow of >5 cm/s with no diastolic reversal suggesting venous insufficiency. Interpretation of Figures 11-18: There is a normal increase in the baseline diameter of the vessel post-papaverine injection with normal peak systolic velocities more than 35 cm/s with continuous end diastolic velocity of more than 5 cm/s with no diastolic reversal. Suggesting venous insufficiency**



**Figure 19: 35 min**

## Complications

94% of the patient studied did not show any complications (Table 8); however, 2 cases out of 33 patients showed priapism. Our findings are similar to a study by Kilic *et al.* where complications of priapism were noted in 18 of the 672 patients studied.<sup>13</sup> The two patients who developed priapism were during the initial part of the study further in the due course of our study to prevent delayed priapism we routinely injected 2 ml of 1:10000 dilution of phenylephrine intracavernosally. Both the cases of priapism did not show any arterial or venous insufficiency.

## CONCLUSION

When arterial insufficiency is found, patients can be considered to have systemic arteriovascular disease. On the other hand, veno-occlusive dysfunction is not correlated with systemic arterial vascular problems. In conclusion, investigating the hemodynamics and direction of flow in the cavernosal artery by color duplex Doppler for ED is not time-consuming and may help establish an accurate diagnosis of vascular causes of impotence.

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# Association of Pre-operative Symptoms with X-ray Abnormalities in Thyroid Swellings

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## Abstract

**Introduction:** Thyroid swelling is a common problem in clinical practice that poses challenges in detecting the type and size of the swelling. Despite the large number of patients the data available on such patients is relatively limited, especially regarding the appropriate pre-operative symptomatic and radiographic assessment.

**Objectives:** To assess, the association of pre-operative symptoms with X-ray abnormalities in thyroid swellings. (1) To study the variation in tracheal position with increase in size of the swelling, (2) to study the symptoms related to increase in the size of the thyroid.

**Materials and Methods:** This study was conducted in 30 patients with thyroid swellings >5 cm in ultrasonography, between 2011 and 2013. The parameters included were: Age, pathological data, radiography, thyroid function tests.

**Results:** In present study, most of the patients fall in the age group of 31-40 years and almost all patients are females, i.e., 26 out of 30 were females and only 4 were males. Of the 30 patients, 15 (50%) had colloid goiter, 8 (26.3%) had multinodular goiter, 4 (13.3%) had nodular goiter, 3 (10%) had papillary carcinoma. 5 patients had tracheal deviation whose severity was categorized as mild, moderate and severe with 2 were mild and severe each.

**Conclusion:** Thyroid swelling is more common in female population. As thyroid swelling increases, tracheal deviation also increases and the severity of tracheal indentation also increase.

**Key words:** Colloid goiter, Multinodular goiter, Nodular goiter, X-ray

## INTRODUCTION

Goiter is enlargement of thyroid gland. It is the most common presentation of thyroid diseases. The word goiter is derived from "guttur," the Latin term for throat.<sup>1</sup> Thyroid swelling is a common problem in clinical practice that poses challenges in detecting the type and size of the swelling. Compressive symptoms are common among patients with thyroid disease and represent an indication for thyroidectomy.<sup>2</sup> Compressive symptoms range from mild, presenting with neck pressure or globus sensation, to

severe, characterized by significant dysphagia or dyspnea. In rare cases, tracheal or esophageal compression leads to acute airway distress that requires emergent treatment with intubation or tracheostomy.<sup>3</sup> Although diffuse thyroid enlargement is associated with tracheoesophageal compression, compressive symptoms are also commonly observed in patients with only mild to moderate thyroid enlargement. In addition to direct compression from an enlarged thyroid gland, dysphagia and shortness of breath may be a manifestation of thyrotoxicosis, Hashimoto thyroiditis, De Quervain thyroiditis, and other inflammatory diseases of the thyroid. Previous studies suggest that inflammation of the thyroid gland may be etiology of compressive symptoms, but this association has not been fully elucidated.<sup>1</sup> Despite the large number of goiter patients and the potential for surgical complications, data available on such patients is relatively limited, especially regarding the appropriate pre-operative symptomatic and radiographic assessment.<sup>4</sup>

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### X-rays

X-rays with photon energies above 5-10 keV (below 0.2-0.1 nm wavelength) are called hard X-rays, while those with lower energy are called soft X-rays.<sup>5</sup> Hard X-rays can traverse relatively thick objects without being much absorbed or scattered. For this reason X-rays are widely used to image the inside of visually opaque objects.

Due to their penetrating ability hard X-rays are widely used to image the inside of objects, e.g, in medical radiography and airport security. X-rays are emitted by electrons; they can be generated by an X-ray tube, a vacuum tube that uses a high voltage to accelerate the electrons released by a hot cathode to a high velocity. The high velocity electrons collide with a metal target, the anode, creating the X-rays. In medical X-ray tubes the target is usually tungsten or a more crack-resistant alloy of rhenium (5%) and tungsten (95%), but sometimes molybdenum for more specialized applications, such as when softer X-rays are needed as in mammography. In crystallography, a copper target is most common, with cobalt often being used when fluorescence from iron content in the sample might otherwise present a problem.

### MATERIALS AND METHODS

Between October 2011 and March 2013, 30 patients of thyroid swellings were taken in present study. Patient's details, pathological data (fine needle aspiration cytology and histopathological examination), radiography (ultrasonography [USG] neck and digital X-ray neck both anteroposterior and lateral views) and serum T3, T4 and thyroid stimulating hormone were recorded from these patients. Size more than 5 cm of the thyroid gland in USG was included in the study. In X-ray neck an arbitrary midline drawn from mentum to suprasternal notch taken and the deviation of trachea from the midline was measured and noted. Compression of the trachea and calcification in the region of thyroid gland were also noted. Patient underwent thyroidectomy and the histopathology was noted in these patients. Size more than 5 cm and physiological goiter were excluded from the study. Patient's details included name, age, sex, history of swelling in the neck, pain in the swelling, difficulty in swallowing and difficulty in breathing (DIB) were noted (Figures 1-9).

Patients presented with huge swellings and compressive symptoms were compared with deviation of the trachea and indentation of trachea in X-ray.

Sample size: 30 patients with thyroid swelling.

#### Inclusion Criteria

- Age >15 years
- Both males and females



Figure 1: Clinical picture of thyroid swelling (Case 1)



Figure 2: Clinical picture of thyroid swelling (Case 2)



Figure 3: Clinical picture of thyroid swelling (Case 3)

- USG size >5 cm
- All thyroid swellings posted for surgery including malignancy.

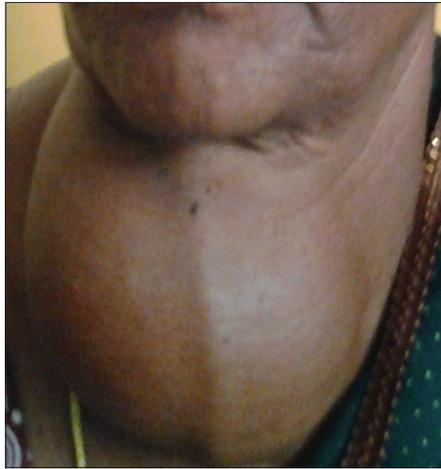


Figure 4: Clinical picture of thyroid swelling (Case 4)



Figure 7: X-ray neck anteroposterior and lateral view (Case 3)



Figure 5: X-ray neck anteroposterior and lateral view (Case 1)

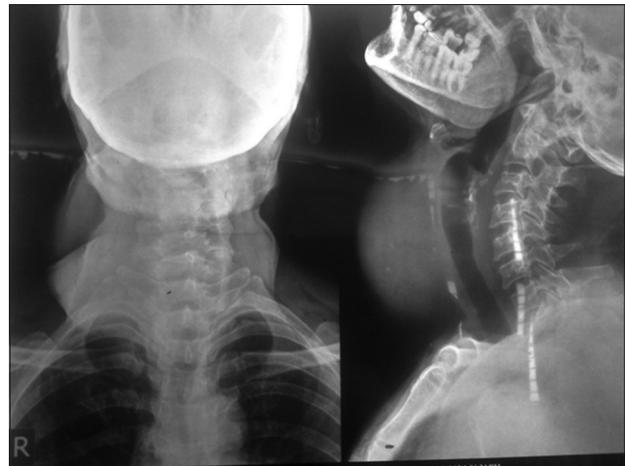


Figure 8: X-ray neck anteroposterior and lateral view (Case 4)



Figure 6: X-ray neck anteroposterior and lateral view (Case 2)

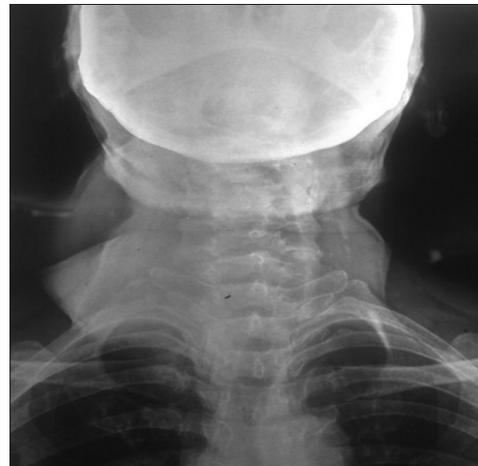


Figure 9: X-ray neck with arbitrary line

#### Exclusion Criteria

- Age <15 years
- Physiological goiter
- USG size <5 cm
- Patients with thyroid swelling who are unfit for surgery.

#### Statistical Methods Applied Are

1. Descriptive
2. Frequency
3. Chi-square test
4. Crosstabs (contingency table analysis).

**Descriptive**

The descriptive 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 (the default).

**Frequencies**

The frequencies procedure provides statistics and graphical displays that are useful for describing many types of variables. For a first look at our data, the frequencies procedure is a good place to start.

**Chi-square Test**

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 (Contingency Table Analysis)**

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. All the statistical calculations were done through SPSS for windows (version 16.0).

**OBSERVATIONS AND RESULTS**

The present study is hospital based prospective study between October 2011 and March 2013. We considered 30 patients in the present study, whose ultrasound size is ≥5 cm. Most of the patients presented with swelling in front of the neck rather than other symptoms.

In present study, most of the patients fall in the age group of 31-40 years and least in <20 years (Table 1).

In present study almost all patients are females, i.e., 26 out of 30 were females and only 4 were males (Table 2).

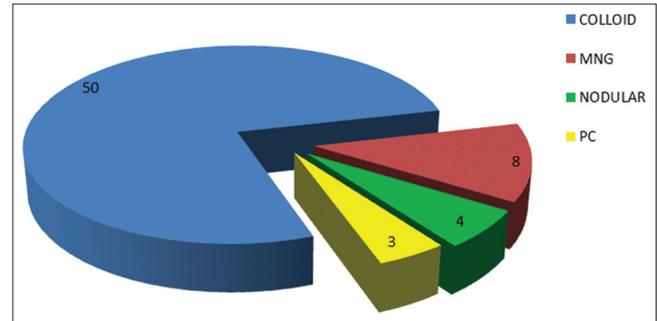
Table 3 shows statistical test applied to check statistically significance between them.

Table 4 and Graph 1 denote distribution of diagnosis of colloid goiter, multinodular goiter (MNG), nodular goiter and papillary carcinoma (PC). The most common type of goiter is colloid goiter and least is PC in present study.

In present study, all patients presented with swelling in front of neck. None presented with difficulty in swallowing (Graph 2).

Most of the patients, i.e., 19 out of 30 in present study has thyroid size (USG size) between 5 and 6 cm. Only 1 lies between 8 and 9 cm (Graph 3).

Table 5 denotes distribution of diagnosis in relation to age among all the types of goiter and PC. In the present study,



Graph 1: Diagnosis distributions

Table 1: Age distribution (n=30)

Age	Frequency	Percentage
<20	2	6.7
21-30	5	16.7
31-40	8	26.6
41-50	6	20.0
51-60	6	20.0
61-70	3	10.0

Table 2: Sex determinations

Sex	Frequency	Percentage
Female	26	86.7
Male	4	13.3

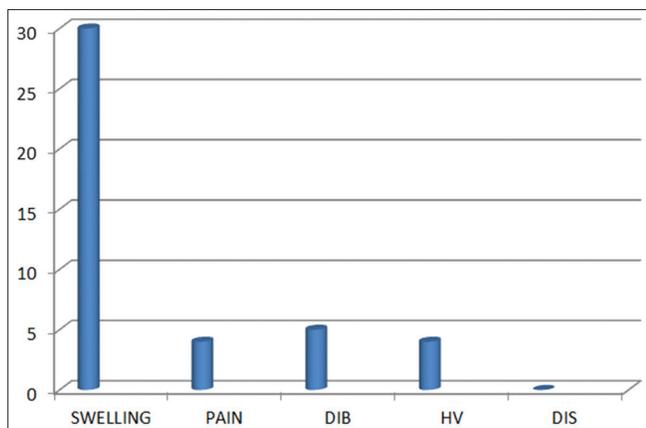
Table 3: Test statistics of age and sex

Test statistics	Age	Sex
Chi-square	4.800	16.133
df	5	1
Asymptotic significance	0.441	0.000 (statistically significant)

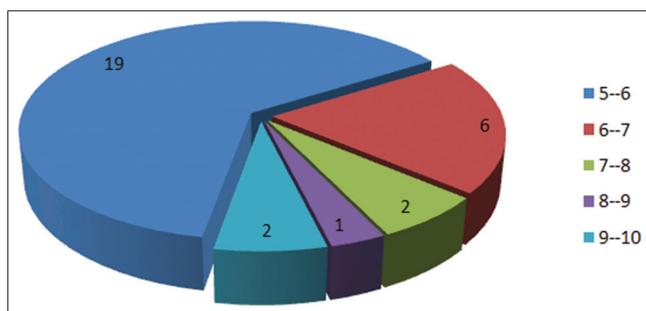
Table 4: Diagnosis distributions

Diagnosis	Frequency	Percentage
Colloid goiter	15	50
MNG	8	26.7
Nodular goiter	4	13.3
PC	3	10

MNG: Multinodular goiter, PC: Papillary carcinoma



Graph 2: Symptoms distribution



Graph 3: Distributions according to ultrasonography size

most common thyroid swelling is colloid and it is presented among the patients who lie between 41 and 50 years.

Among 19 patients whose size lies between 5 and 6 cm, 5 of them fall in the age group of 31-40 years (Table 6).

Table 7 denotes distribution of diagnosis in relation to sex. 13 among 26 females and 2 among 4 males presented as colloid goiter. Other 2 males presented as PC.

Table 8 denotes relations of USG size and DIB 2 each among 5 patients, who presented with DIB, have their thyroid size between 7-8 cm and 9-10 cm.

Table 9 shows relations of USG size and pain. 2 among 4, who presented with pain, have their size between 9 and 10 cm.

Table 10 shows relation of USG size and hoarseness of voice. 2 among 4 patients, who presented with hoarseness of voice, have their thyroid size between 9 and 10 cm.

Table 11 shows correlation of USG size and TD. Size of the thyroid and tracheal deviation in X-ray has linear correlation.

Table 12 shows distribution of tracheal indentation (TI) according to size. As size of thyroid increases, TI also increases.

Table 5: Distribution of diagnosis in relation to age

Age	Diagnosis				Total
	Colloid	MNG	Nodular	PC	
<20					
Frequency	2	0	0	0	2
Percentage	100.0	0.0	0.0	0.0	100.0
21-30					
Frequency	2	2	1	0	5
Percentage	40.0	40.0	20.0	0.0	100.0
31-40					
Frequency	4	1	1	2	8
Percentage	50.0	12.5	12.5	25.0	100.0
41-50					
Frequency	5	1	0	0	6
Percentage	83.3	16.7	0.0	0.0	100.0
51-60					
Frequency	2	3	1	0	6
Percentage	33.3	50.0	16.7	0.0	100.0
61-70					
Frequency	0	1	1	1	3
Percentage	0.0	33.3	33.3	33.3	100.0
Total					
Frequency	15	8	4	3	30
Percentage	50.0	26.7	13.3	10.0	100.0

MNG: Multinodular goiter, PC: Papillary carcinoma

Table 6: Distribution according to USG size and age

Age	USG size					Total
	5-6	6-7	7-8	8-9	9-10	
<20						
Frequency	2	0	0	0	0	2
Percentage	100.0	0	0	0	0	100.0
21-30						
Frequency	4	1	0	0	0	5
Percentage	80.0	20.0	0	0	0	100.0
31-40						
Frequency	5	2	0	1	0	8
Percentage	62.5	25.0	0	12.5	0	100.0
41-50						
Frequency	4	0	0	0	2	6
Percentage	66.7	0	0	0	33.3	100.0
51-60						
Frequency	2	3	1	0	0	6
Percentage	33.3	50.0	16.7	0.0	0.0	100.0
61-70						
Frequency	2	0	1	0	0	3
Percentage	66.7	0	33.3	0	0	100.0
Total						
Frequency	19	6	2	1	2	30
Percentage	63.3	20.0	6.7	3.3	6.7	100.0

USG: Ultrasonography

## DISCUSSION

Goiter is an enlargement of thyroid gland. It may be euthyroid, hypothyroid or hyperthyroid. It's a process of progressive enlargement. This progression causes compressive symptoms such as DIB, pain, hoarseness of voice, difficulty in swallowing. Compressive symptoms are common in thyroid disease.

**Table 7: Distribution of diagnosis in relation to sex**

Sex	Diagnosis				Total
	Colloid	MNG	Nodular	PC	
Male					
Frequency	2	0	0	2	4
Percentage	50.0	0	0	50.0	100.0
Female					
Frequency	13	8	4	1	26
Percentage	50.0	30.8	15.4	3.8	100.0
Total					
Frequency	15	8	4	3	30
Percentage	50.0	26.7	13.3	10.0	100.0

MNG: Multinodular goiter, PC: Papillary carcinoma

**Table 8: Relations of USG size and DIB**

DIB	USG					Total
	5-6	6-7	7-8	8-9	9-10	
No						
Frequency	19	6	0	0	0	25
Percentage	76.0	24.0	0	0	0	100.0
Yes						
Frequency	0	0	2	1	2	5
Percentage	0	0	40.0	20.0	40.0	100.0
Total						
Frequency	19	6	2	1	2	30
Percentage	63.3	20.0	6.7	3.3	6.7	100.0

USG: Ultrasonography, DIB: Difficulty in breathing

**Table 9: Relations of USG size and pain**

Pain	USG					Total
	5-6	6-7	7-8	8-9	9-10	
No						
Frequency	19	5	1	1	0	26
Percentage	73.1	19.2	3.8	3.8	0	100.0
Yes						
Frequency	0	1	1	0	2	4
Percentage	0	25.0	25.0	0	50.0	100.0
Total						
Frequency	19	6	2	1	2	30
Percentage	63.3	20.0	6.7	3.3	6.7	100.0

USG: Ultrasonography

Goiter is the most prevalent endocrine condition in the world affecting over 500 million with prevalence rates reaching up to 30%.<sup>6,7</sup> Local symptoms in patients with euthyroid goiter undergoing surgery have been reported to vary between 13% and 50%.<sup>8,9</sup>

The neck and throat symptoms in patients with goiter have been invariably attributed to the glandular hypertrophy of the thyroid and its mass effect on the laryngotracheal framework.<sup>10</sup>

Compression and invasion of the laryngotracheal complex may also result in airway symptoms with narrowing of the lumen and or impaired mobility of the vocal fold with or without recurrent laryngeal nerve neuropathy.<sup>7</sup>

**Table 10: Relation of USG size and hoarseness of voice**

Hoarseness of voice	USG size					Total
	5-6	6-7	7-8	8-9	9-10	
No						
Frequency	18	6	2	0	0	26
Percentage	69.2	23.1	7.7	0	0	100.0
Yes						
Frequency	1	0	0	1	2	4
Percentage	25.0	0	0	25.0	50.0	100.0
Total						
Frequency	19	6	2	1	2	30
Percentage	63.3	20.0	6.7	3.3	6.7	100.0

USG: Ultrasonography

**Table 11: Correlation of USG size and TD**

Correlations	USG	TD
USG		
Pearson correlation	1	0.952 (**)
Significance (two-tailed)	0.000	
<i>n</i>	30	30
TD		
Pearson correlation	0.952 (**)	1
Significance (two-tailed)	0.000	
<i>n</i>	30	30

\*\*High correlation at 0.01 (two-tailed). USG: Ultrasonography, TD: Tracheal deviation

**Table 12: Distribution of TI according to size**

TI	USG					Total
	5-6	6-7	7-8	8-9	9-10	
No						
Frequency	19	6	0	0	0	25
Percentage	76.0	24.0	0	0	0	100.0
Yes						
Frequency	0	0	2	1	2	5
Percentage	0	0	40.0	20.0	40.0	100.0
Total						
Frequency	19	6	2	1	2	30
Percentage	63.3	20.0	6.7	3.3	6.7	100.0

USG: Ultrasonography, TI: Tracheal indentation

In a series of over 3,000 thyroidectomies, Lacoste *et al.* found that 11% of patients complained of compressive symptoms.<sup>11</sup>

MNG, one of the more common indications for thyroidectomy, is associated with compressive symptoms. In a 7 years series, 33% of patients diagnosed with benign goiter had compressive symptomatology.<sup>12</sup>

A separate study focusing on marked thyroid gland enlargement reported an incidence of compressive symptoms around 86%.<sup>13</sup>

Present study included 30 patients, who presented with swelling in front of the neck. Among them 8 patients were under the age group of 31-40 years, 6 patients each

were in the age group of 41-50 years and 51-60 years and 2 patients were <20 years.<sup>14</sup> Among 30 patients 26 were females, i.e., 86.7% of the study were females.

Table 13 shows the comparison done between present study and other two studies which shows percentage of females.

All patients presented with swelling in front of neck. 5 out of 30 presented with DIB. It accounts for 16.7%. 4 out of 30 presented with pain, i.e., 13.3% and 4 presented with hoarseness of voice, i.e., 13.3%.

Shin *et al.*<sup>12</sup> showed in his work that 85% presented with swelling in front of the neck and 49.7% presented with DIB and 3.5% with hoarseness of voice.

15 patients were diagnosed to have colloid goiter, i.e., 50% had colloid goiter. Eight were diagnosed to have MNG, i.e., 26.7%. 4 out of 30 were diagnosed to have nodular goiter, i.e., 13.3% and 3 had PC, i.e., 10%. 19 patients among 30 had their thyroid size between 5 and 6 cm in ultrasound. It accounts for 63.3%. Six had between 6 and 7 cm, i.e., 20%. Two between 7 and 8 cm and 2 between 9 and 10 cm. Among 8 patients in the age group of 31-40 years, 6 were females, i.e. 20% of females was in the age group of 31-40 years. Five means 16.6% of females in the age group of 41-50 years. Most common presentation in present study was colloid goiter, i.e among 15 colloid goiter patients 5 (33.3%) were in the age group of 41-50 years and 13 were females and 2 were males. Among 3 patients with PC, 2 were males and all the 8 patients with MNG were females.

Two patients with the thyroid size on ultrasound between 9 and 10 cm presented with DIB, pain and hoarseness of voice each. Two patients with size between 7 and 8 cm presented with DIB and pain. One patient with size between 5 and 6 cm presented with hoarseness of voice was diagnosed as PC.

There was a linear correlation between size of the thyroid on ultrasound and tracheal deviation on X-ray. Five patients had tracheal deviation whose severity was categorized as mild moderate and severe with two were mild and severe each.

Fiorentino *et al.* examined this very overlap of symptoms by conducting a study on 25 goiter patients who complained

of local neck symptoms (throat discomfort, dysphagia, hoarseness).<sup>14</sup>

Gittoes *et al.*<sup>15</sup> have shown that upper airway obstruction occurs in about one-third of patients with goiter seen in general medical endocrinology clinics, emphasizing the importance of optimal airway evaluation in goiter patients.

Shin *et al.* in their retrospective study on pre-operative evaluation of surgery on goiter done on 200 patients. Common presenting symptoms in their series included shortness of breath (approximately 50%) and dysphagia (approximately 50%), emphasizing the effect of cervical and substernal goiter on the adjacent cervical viscera. Multivariate analysis showed that the presence of shortness of breath was related to goiter size. Furthermore, the presence of shortness of breath was significantly related to the imaging finding of tracheal compression. Thus, clearly there is a relationship between shortness of breath, goiter size, and tracheal compression. Because of this relationship between shortness of breath and the objective computed tomography (CT) scan radiographic finding of tracheal compression, tracheal compression appears to be an important radiographic finding. Therefore, the pre-operative radiographic finding of tracheal compression is an appropriate surgical indication.<sup>16</sup>

Mellisant CF *et al.* showed in their prospective study 28 female patients with a goitre and without pulmonary disorders. Lung function measurements consisted of maximum expiratory and inspiratory flow-volume curves and of airway resistance. CT-scans and X-rays were performed during apnea at functional residual capacity. Almost all lung function tests were significantly correlated with each other. CT-scans and X-ray was significantly correlated to each other only the correlation between the tracheal narrowing measured with CT-scan and X-ray was significant.<sup>17</sup>

The obstruction due to enlarged thyroid can be dangerous because of narrowing of the trachea and the development of tracheitis with edema and tracheomalacia, leading to severe narrowing of the airway with serious obstruction resulting in a respiratory emergency.<sup>18</sup>

The main indications for surgery in thyroid disease include fear of malignancy, tracheoesophageal compression, and cosmetic reasons.<sup>19</sup> Multiple studies have demonstrated improvement or resolution of compressive symptoms after thyroid surgery. Carolin *et al.* showed in their study a large series of patients with compressive symptoms secondary to thyroid disease. In the study, 85% of patients with pre-operative compressive symptoms had resolution of compressive symptoms after thyroidectomy.<sup>20</sup>

**Table 13: Comparison with other studies**

Sex	Present study	Shin <i>et al.</i> <sup>12</sup>	Gittoes <i>et al.</i> <sup>15</sup>
Females (%)	26 (86.7)	130 (65)	134 (87.5)

Present study may have limitations as we have taken arbitrary line for the measurement of tracheal deviation.

## CONCLUSION

The present study helps to arrive at several conclusions which are as follows:

- Thyroid swelling is more common in female population
- Colloid goiter is the most common presentation irrespective of age and sex
- If male patients present with thyroid swelling, malignancy has to be ruled out
- Male patients are at high risk for PC
- As thyroid swelling increases, tracheal deviation also increases
- As thyroid swelling increases, the severity of TI also increase
- As thyroid swelling increases, symptoms also increase
- Helps in pre and post-operative evaluation.

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# High-Resolution Computed Tomography Chest Findings and Correlation with CD4 Cell Counts among Human Immunodeficiency Virus-Infected Children Presenting with Digital Clubbing, Chronic Cough and Crackles in Chest

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## Abstract

**Background:** Digital clubbing is an important presentation in the human immunodeficiency virus (HIV) infected children especially with the chronic invasive fungal lung diseases. High-resolution computed tomography (HRCT) chest plays an increasing important complementary role in establishing an accurate diagnosis when chest X-ray (CXR) findings are equivocal or non-specific.

**Materials and Methods:** Three hundred HIV-infected children enrolled for the present study and the children presenting with digital clubbing, chronic cough, and crackles in chest were selected. The retrospective analysis of all the CD4 cell counts, before and during antiretroviral therapy (ART) of the selected patients was done. All the selected children were referred for CXR, HRCT chest and sputum for fungal element staining and culture.

**Results:** Eight (2.66%) children out of the 300 HIV-infected children were presenting with digital clubbing, chronic cough, and extensive crackles in the chest. A definitive microbiological diagnosis of fungal infections was made from the sputum fungal element staining and cultures in 7 (87.5%) patients out of the selected 8 patients, which included *Aspergillus fumigatus* in 3, *Cryptococcus neoformans* in 2 and *Candida albicans* in 2 patients. The mean of lowest CD4 cell counts, before and during ART up to the time of examination of the selected 8 children was 137.87 cells/ $\mu$ l ( $\pm$ 76.53). The means of lowest CD4 cell counts of 3 cases of pulmonary aspergillosis, 2 cases of pulmonary cryptococcosis, and 2 cases of pulmonary candidiasis were 93.6 cells/ $\mu$ l ( $\pm$ 5.03), 114 cells/ $\mu$ l ( $\pm$ 14.14), and 137 cells/ $\mu$ l ( $\pm$ 24.04), respectively. The HRCT chest images of all the above selected 8 children were showing with findings suggestive of fungal lung infections.

**Conclusion:** Digital clubbing, chronic cough, and extensive crackles in chest were the strong clinical findings suggestive of invasive fungal lung infections among HIV-infected children. HRCT chest findings of pulmonary fungal infection were diverse, but some characteristic HRCT chest findings were highly suggestive of pulmonary fungal infections in immunocompromised patients.

**Key words:** Acquire immunodeficiency syndrome, Clubbing, Human immunodeficiency virus, Imaging lung, Lung diseases-fungal

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## INTRODUCTION

Many children were infected with human immunodeficiency virus (HIV). The majority of them were transmitted through parents to child transmission. As of now, with the advances in the knowledge of the disease and its management including antiretroviral therapy (ART), many

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of the HIV-infected children on ART are living longer in good health as chronic manageable diseases. Some of them who are having low CD4 cell counts due to delay in starting of ART as per guideline or who are getting resistance to ART especially due to poor adherence to ART are having high risk for HIV-related opportunistic infections, like chronic fungal infections of lung. Opportunistic fungal infections still remain a problem in HIV-infected children. These fungal infected patients have increased morbidity and mortality as any other chronic disease. Necropsy studies in acquire immunodeficiency syndrome (AIDS) patients have confirmed an incidence of fungal infection of 20-49%.<sup>1,2</sup> However, these patients are subjected to wide spectrum of pathogens; fungal infections play an important role. As these infections differ in different geographical boundaries, knowledge about the spectrum of them is crucial for clinicians.<sup>3,4</sup> Invasive fungal infections are common opportunistic infection and the risk of invasive fungal infection varies with host immunity, as well as environmental exposure.<sup>5</sup> Improved skills and availability of fungal diagnostic tests would improve the outcome in the management of opportunistic infections. Knowledge regarding the opportunistic fungal infections will be useful as timely recognition and treatment of opportunistic infections are the only option. Digital clubbing is an important presentation in the HIV-infected children especially with the chronic invasive fungal lung diseases. Computed tomography (CT) has advantages over chest radiology as it is more sensitive and specific for a variety of conditions affecting the pulmonary parenchyma. High-resolution CT (HRCT) examination of chest was more sensitive (could detect abnormalities when the chest radiography was normal); showed greater accuracy in characterizing disease into interstitial, airway and air space process; and gave a more accurate depiction of the extent of disease. The radiation dose is an important consideration in children; therefore, CT does not have a role in the investigation of a single, uncomplicated lower respiratory tract infection in an immunocompetent child. HRCT chest plays an increasing important complementary role in establishing an accurate diagnosis when chest X-ray (CXR) findings are equivocal or non-specific. So in view of such a situation, this present study was conducted to know the HRCT chest findings and correlation with CD4 cell counts among HIV-infected children presenting with digital clubbing, chronic cough and crackles in chest, at the Department of Pediatrics, Jawaharlal Nehru Institute of Medical Sciences (JNIMS), Manipur, India.

## MATERIALS AND METHODS

This present study was conducted at the Department of Pediatrics, JNIMS, over a period of 4 years from September

2010 to August 2014. The study was approved by the Institutional Ethical Committee of JNIMS.

As inclusion criteria, all the HIV infected children of both sexes with or without ART in the age group of 18 months to 15 years attended the outpatient department (OPD) of pediatrics; JNIMS were enrolled in the present study.

As exclusion criteria, all the HIV infected children of both sexes below 18 months and above 15 years of age were excluded. A written informed consent was obtained from the parents or caregiver of each child before enrollment in the present study. The confidentiality of all the children was maintained.

The HIV status of all the patients was confirmed by the three antibody tests at the integrated counseling and testing centers approved by the National AIDS Control Organization (NACO), Ministry of Health and Family Welfare, Government of India.

All the CD4 cell counts of all the patients enrolled in our study were determined by the CD4 machines, approved by the NACO. Three hundred HIV positive children were evaluated by a pre-designed protocol covering the patient's particulars, relevant past history, clinical conditions before and during ART, adherence to ART, high-risk behavior, presenting complaints and clinical examinations, duration of cough, extension of crackles in chest. Those children presenting with digital clubbing, chronic cough and crackles in chest were selected from the 300 HIV-infected children after thorough clinical examinations. All the CD4 cell counts before and during ART of the selected patients were analyzed retrospectively. The selected patients were referred for CXR, HRCT chest at the Department of Radiodiagnosis, JNIMS. Early morning expectorated sputum samples of the selected patients were collected with complete universal precautions for direct microscopic examinations using Gram- and Giemsa-staining, KOH mounts, India ink preparations and fungal culture at the Department of Microbiology, JNIMS. The samples were subjected to direct microscopy using Gram- and Giemsa-staining, KOH mounts and India ink preparations. Relevant methods were used for fungal culture, isolation and diagnosis which included a battery of tests as per standard procedures.

## RESULTS

Three hundred HIV-infected children of both sexes with or without ART in the age group of 18 months to 15 years attended the pediatrics OPD of JNIMS were enrolled in the present study over a period of 4-year.

Eight (2.6%) children out of the 300 HIV-infected children presented with digital clubbing, chronic cough, and extensive crackles in chest.

The male:female ratio of the selected eight patients was 1:3 (Table 1).

A definitive microbiological diagnosis of fungal infections was made from the sputum fungal element staining and cultures in 7 (87.5%) patients out of the selected 8 patients, which included *Aspergillus fumigatus* in 3, *Cryptococcus neoformans* in, 2 and *Candida albicans* in 2 patients. The mean of lowest CD4 cell counts, before and during ART up to the time of examination of the selected 8 children was 137.87 cells/ $\mu$ l ( $\pm$ 76.53) (Table 2). The mean of lowest CD4 cell counts of 3 cases of pulmonary aspergillosis, 2 cases of pulmonary cryptococcosis, and 2 cases of pulmonary Candidiasis were 93.6 cells/ $\mu$ l ( $\pm$ 5.03), 114 cells/ $\mu$ l ( $\pm$ 14.14), and 137 cells/ $\mu$ l ( $\pm$ 24.04), respectively, (Table 2 and Figures 1-8).

One patient out of the selected 8 children shows negative fungal result in the sputum of fungal element staining and culture. The CD4 cell count of the patient was 320 cells/ml (Table 2).

The HRCT chest images of all the selected 8 children were showing with findings suggestive of fungal lung infections.

**Table 1: Demographic profile of the selected 8 patients**

Age in months/years	Male	Female	Total number of male and female
18 months-2 years			
>2-5 years		1	1
>5-10 years		2	2
>10-15 years	2	3	5
Total	2	6	8

**Table 2: Distribution of various opportunistic fungal infections of chest and mean of lowest CD4 cell counts of the selected 8 children**

Opportunistic fungal infection	Total number patients	Mean of lowest CD4 ( $\pm$ SD) cells/ $\mu$ l	Lowest CD4 cells/ $\mu$ l
Pulmonary aspergillosis	3	93.6 ( $\pm$ 5.03)	89, 93, 99
Pulmonary cryptococcosis	2	114 ( $\pm$ 14.14)	104, 124
Pulmonary candidiasis	2	137 ( $\pm$ 24.04)	120, 154
No fungal element isolated	1		320
Total	8	137.87 ( $\pm$ 76.53)	89, 93, 99, 104, 124, 120, 154, 320

SD: Standard deviation

HRCT chest findings of the selected 8 patients presenting with digital clubbing, chronic cough and extensive crackles in chest are as follows.

## DISCUSSION

In the present study, 3 cases of pulmonary aspergillosis were detected and had a mean of lowest CD4 cell counts of 93.6 cells/ $\mu$ l ( $\pm$ 5.03). According to one study, patients who had HIV-associated aspergillosis typically have CD4+ counts <100 cells/ $\mu$ l.<sup>5,6</sup> The findings of the present study are comparable to this, in terms of CD4 counts.

One study reported pulmonary cryptococcal infection in 3.3% cases and occurred at mean CD4 count of 144.5 cells/ $\mu$ l.<sup>7</sup> In another study two patients had pulmonary cryptococcosis. The CD4 counts of these 2 patients were 104 and 143 cells/ $\mu$ l.<sup>8</sup> In the present study 2 patients of pulmonary cryptococcal infection were diagnosed and the mean of the lowest CD4 counts was 114  $\pm$  14.14 cells/ml. The finding of the present study is comparable to this, in terms of CD4 counts.

According to one study *C. albicans* and *Candida glabrata* were isolated from 3 to 1 patient respectively. The mean CD4 cell count was 134.2 cells/ $\mu$ l ( $\pm$ 66.7).<sup>8</sup> In the present study 2 patients of pulmonary candidiasis were diagnosed, and the mean of the lowest CD4 counts was 137 cells/ $\mu$ l ( $\pm$ 24.04). The finding is comparable to this, in terms of CD4 counts.

Angioinvasive disease of aspergillosis is most common, manifest as thick walled cavitary lesions predominating in the upper lobes, with air crescents surrounding areas of desquamated infarcted lung. Less-common patterns include nodules with a peripheral halo of ground-glass attenuation and isolated airway disease or allergic bronchopulmonary aspergillosis, manifesting as bilateral lower lobe consolidation, bronchiectasis, and airway inpaction or “finger in glove.”<sup>9,10</sup>

In the present study the HRCT chest images of the three patients of pulmonary aspergillosis show extensive ground glass opacities (GGO) and mosaic pattern, small cystic lesions, cystic and traction bronchiectasis, peribronchial cuffing, branching nodules, multiple small nodules with subtle peripheral halo, well capsulated cavitary lesion with dense nodule with air crescent suggestive of fungal ball.

In the present study, the HRCT chest images of the two pulmonary cryptococcosis show air trapping mosaic and GGO associated with cystic and cylindrical bronchiectasis, peribronchial cuffing with scattered ground glass appearance.

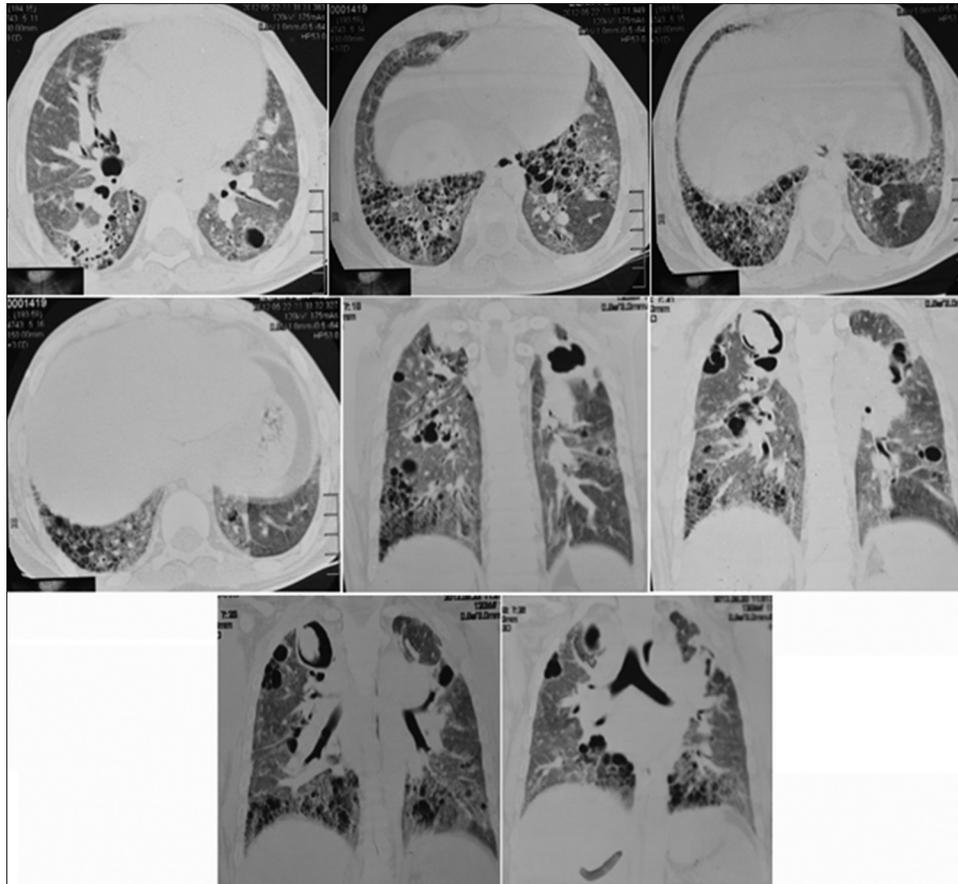


Figure 1: High-resolution computed tomography (HRCT) chest images of a 12-year-old female patient, who had a CD4 cell count as low as 93 cells/ $\mu$ l and *Aspergillus fumigatus* was isolated from her sputum. The HRCT chest images show diffused ground glass opacities in bilateral lung fields with multiple cystic bronchiectasis. Well encapsulated cavitory lesion with dense nodules suggestive of fungal ball involving in right upper lobe also seen

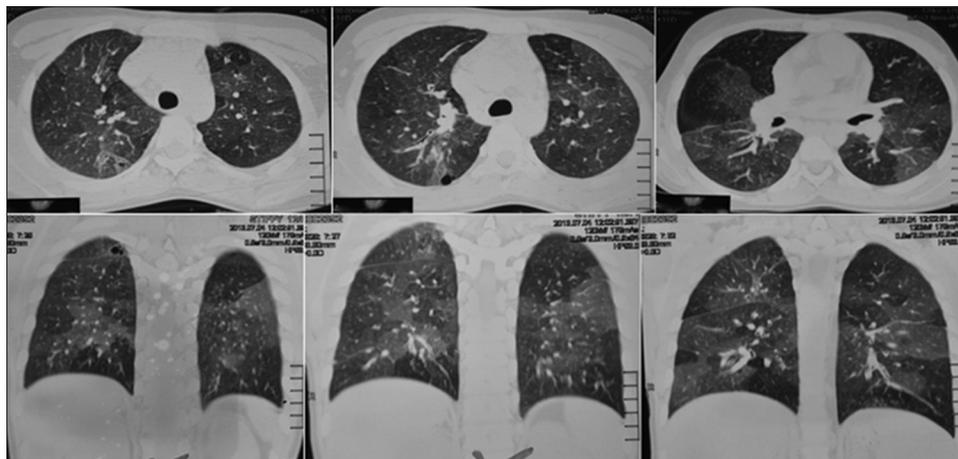


Figure 2: High-resolution computed tomography (HRCT) chest images of a 10-year-old female patient, who had a CD4 cell count as low as 89 cells/ $\mu$ l and *Aspergillus fumigatus* was isolated from her sputum. HRCT chest images show extensive bilateral ground glass opacities are seen with scattered areas of normal and less involved lung parenchyma resulting mosaic pattern. Small cystic lesions are seen in right upper lobe posterior segments

Imaging findings of *Cryptococcus* infection of the chest are varied and non-specific. Reticular or reticulonodular infiltrates are the most common pattern.<sup>9,10</sup> Solitary or multiple nodules, often up to 4 cm in diameter, are seen

in around 30%. A biopsy is usually required for diagnosis. Cavitations occur less frequently in AIDS-related disease compared to immune competent hosts, usually appearing early in the course of the illness, when the level of immune

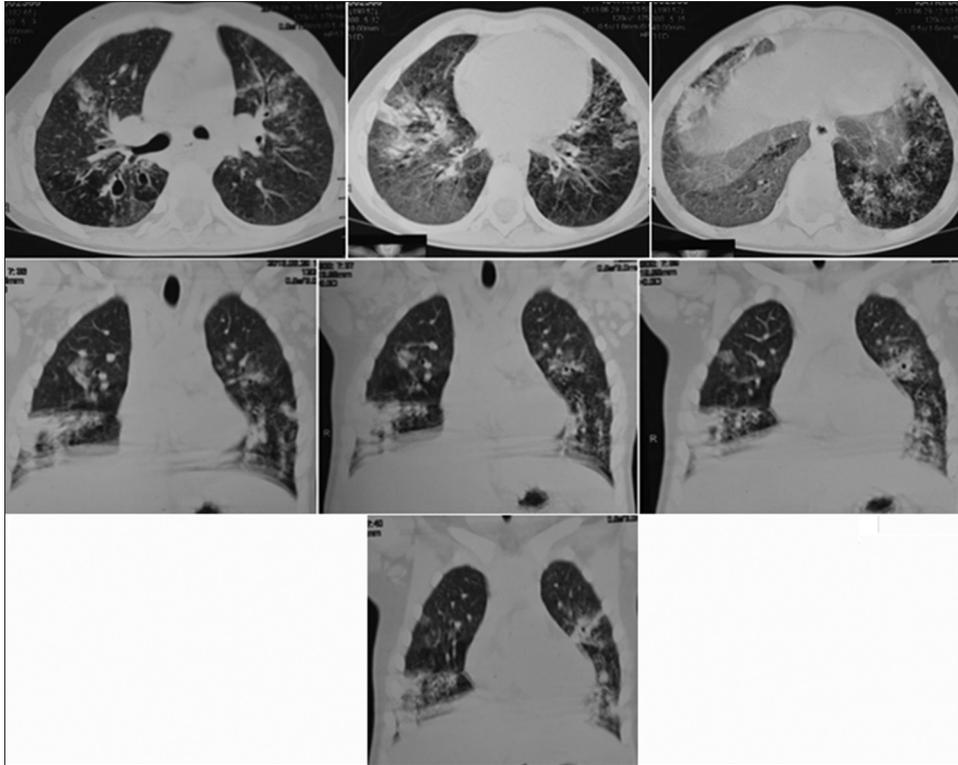


Figure 3: High-resolution computed tomography (HRCT) chest images of a 5-year-old female patient, who had a CD4 cell count as low as 99 cells/ $\mu$ l and *Aspergillus fumigatus* was isolated from her sputum. HRCT chest images show cystic and traction bronchiectasis, peribronchovascular thickening, branching nodules and ground glass appearances are seen in the bilateral upper lobes predominantly in the anterior segments. Similar lesions are seen in the posterior basal segment of bilateral lower lobes. Multiple small nodules with subtle peripheral halo are seen in bilateral upper lobes. Intra and interlobular septal thickening with ground glass appearance is seen predominant in lateral basal segments bilaterally. No significant lymphadenopathy is seen

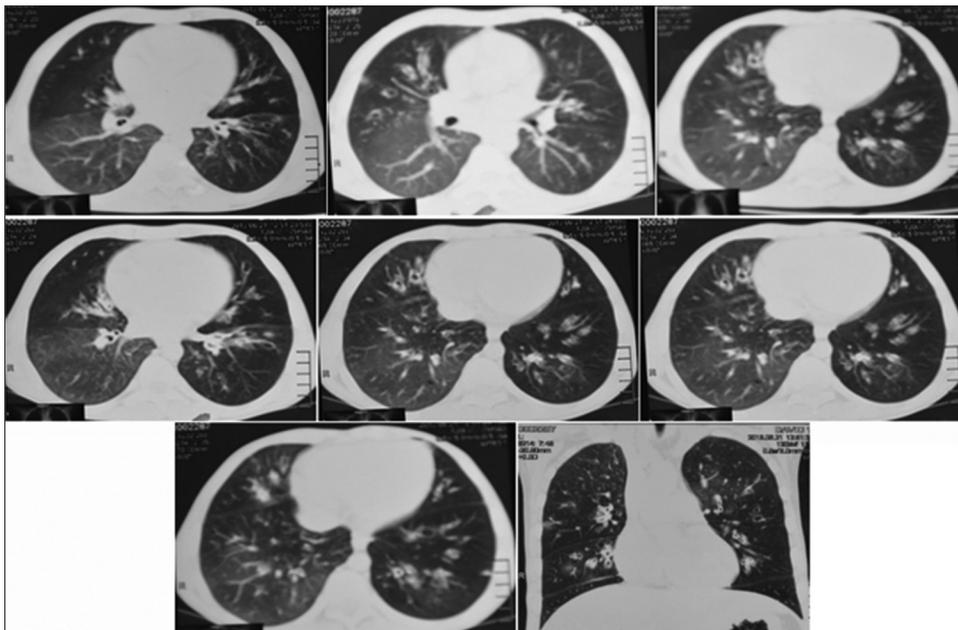
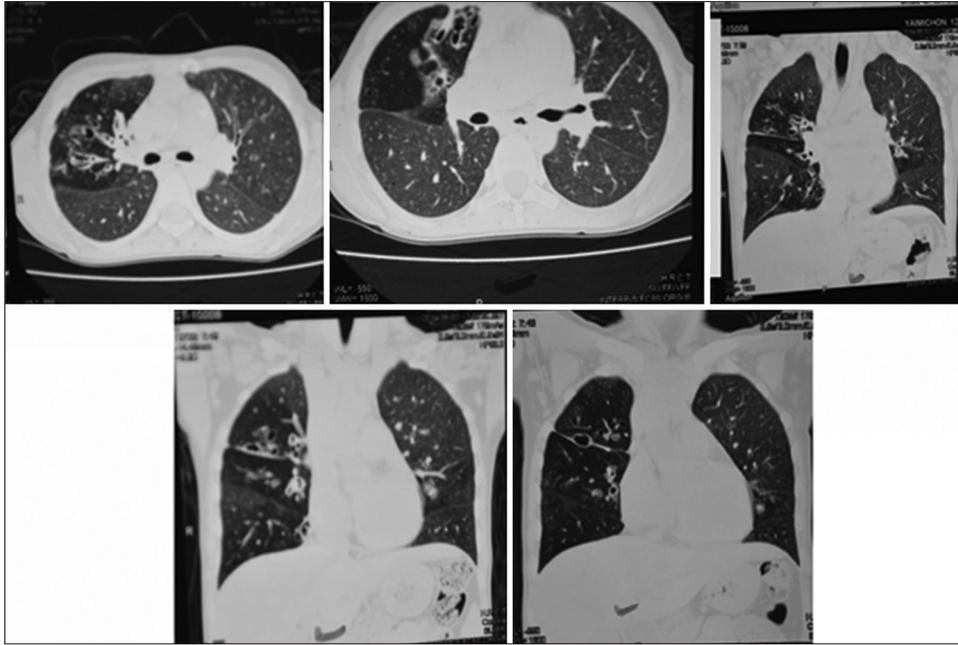
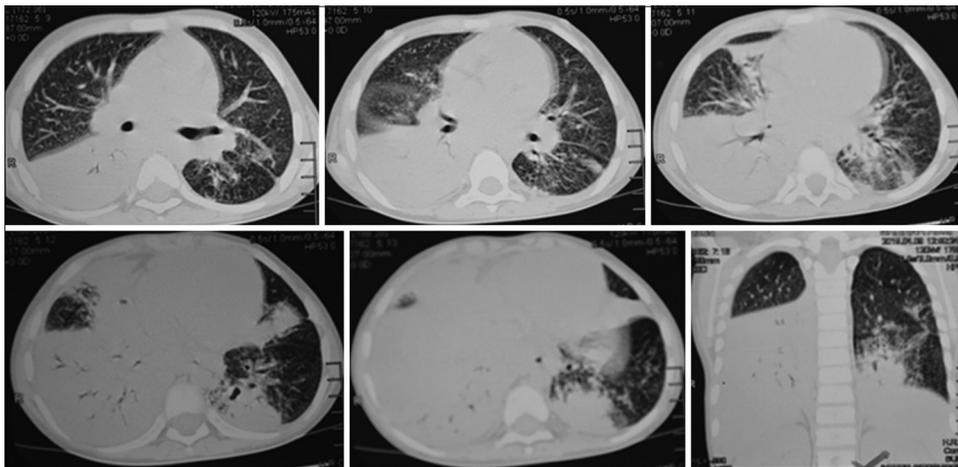


Figure 4: High-resolution computed tomography (HRCT) chest images of a 5-year-old male patient, who had a CD4 cell count as low as 124 cells/ $\mu$ l and *Cryptococcus neoformans* was isolated from his sputum. HRCT chest images show cystic and cylindrical bronchiectasis with peribronchovascular thickening predominantly involving in the bilateral lung upper and lower lobes with scattered ground glass appearance in the bilateral lung fields



**Figure 5:** High-resolution computed tomography (HRCT) chest image of a 12-year-old female patient, who had a CD4 cell count as low as 104 cells/ $\mu$ l and *Cryptococcus neoformans* was isolated from her sputum. HRCT chest images show air trapping mosaic and ground glass opacities attenuation associated with cystic and cylindrical bronchiectasis predominantly in the upper lobes of right lung. Subpleural interstitial thickening pulmonary fibrosis also noted in the right apical-posterior segment. Left lingual subsegmental cystic bronchiectasis is seen with air trapping mosaic attenuation

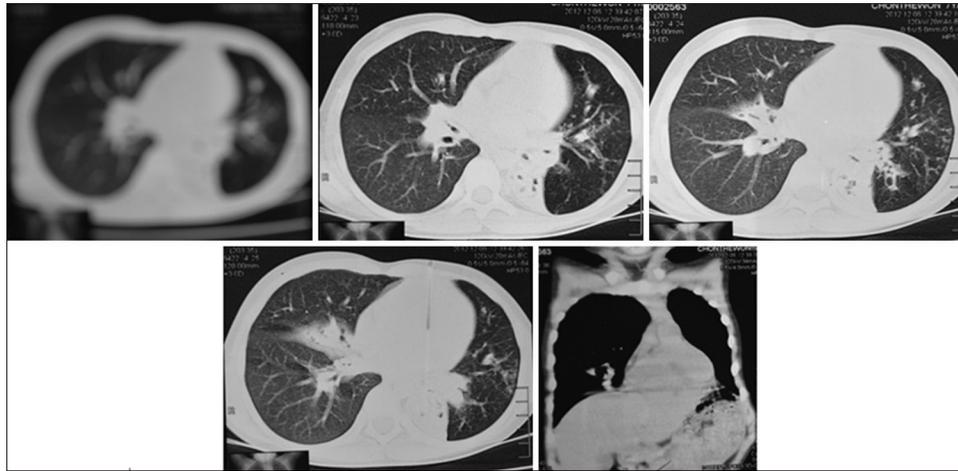


**Figure 6:** High-resolution computed tomography (HRCT) chest image of a 7-year-old female patient, who had a CD4 cell count as low as 154 cells/ $\mu$ l and *Candida albicans*, *Aspergillus* was isolated from her sputum. HRCT chest images show lobar consolidation with the presence of air bronchogram in right lower lobe of the lung. Segmental areas of consolidation are seen in the medial segment of middle lobe, inferior lingual segment and posterior basal segment of left lower lobe. Diffused ground glass opacity of the visualized lung field with patchy normal areas is seen

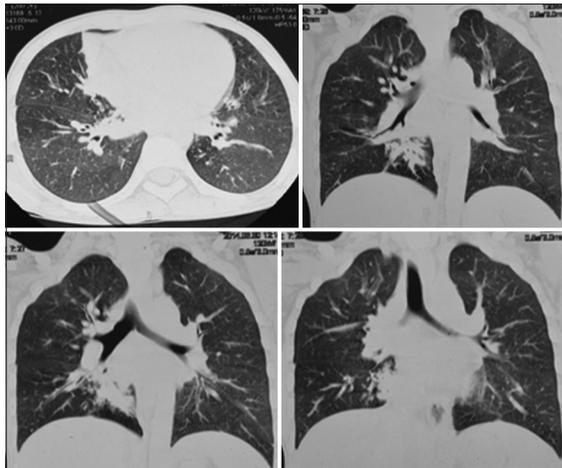
suppression is mild.<sup>6,9,10</sup> Less frequent manifestations of *Cryptococcus* infection of chest include adenopathy effusion, consolidation, millary nodularity and GGO and chest wall abscess.<sup>6,9</sup> The classic appearance is of bilateral symmetric perihilar or diffuse interstitial opacification, which may be reticular, finely granular or ground-glass in appearance. If left untreated, this may progress to alveolar consolidation in 3 or 4 days. Infiltrates clear within 2 weeks but in a proportion, infection will be followed by coarse reticular

opacification and fibrosis.<sup>11</sup> The presence of large nodules and visualization of holo-sign are most suggestive of fungal infection.

The HRCT images of two pulmonary candidiasis in this study show lobar consolidation, dense attenuating parenchymal lesions with air bronchogram, traction bronchiectasis, ground glass appearances (GGO), and centrilobular nodules.



**Figure 7: High-resolution computed tomography (HRCT) chest images of a 7-year-old female patient, who had a CD4 cell count as low as 120 cells/ $\mu$ l and isolated *Candida albicans* *Aspergillus* from sputum. HRCT chest images show parenchymal dense attenuative lesions with air-bronchogram involving the superior segment of the left lower lobe. Another wedge shaped dense attenuating parenchymal lesion is also seen in medial segment of right middle lobe**



**Figure 8: High-resolution computed tomography (HRCT) chest images of a 13-year-old male patient, who had a CD4 cell count as low as 320 cells/ $\mu$ l and fungal element was not isolated from his sputum. HRCT chest images show a wedge shaped parenchymal lesion in medial segment of right middle lobe seen suggestive of consolidation**

In some studies, the HRCT chest typical findings of pulmonary candidiasis are nodules with halo sign. This feature is almost identical to that of invasive pulmonary aspergillosis (IPA), and it is often difficult to distinguish. The nodules of pulmonary candidiasis are usually smaller than those in IPA. In the endobronchial spread, centrilobular nodules, tree-in-bud pattern and peribronchial consolidation are seen.

The HRCT image of a 13-year-old male patient out of the selected 8 children shows a wedge shaped parenchymal lesion in medial segment of right middle lobe seen suggestive of consolidation but fungal element cannot be isolated from the sputum of the patient.

## CONCLUSION

Digital clubbing, chronic cough and extensive crackles in chest were the strong clinical findings suggestive of invasive fungal lung infections among the HIV-infected children. HRCT chest may be considered for these patients with high index of suspicion for fungal chest infections. HIV-positive children with fungal infections of the lung were significantly associated with low CD4 cell counts below 200 cells/ $\mu$ l, the mean of lowest CD4 cell counts was 137.87 cells/ $\mu$ l ( $\pm$ 76.53). This may be due to either delay in starting ART as per the latest national ART guideline of CD4 cell count which was increased from 200 to 350 cells/ $\mu$ l or getting resistance to ART during treatment, especially with poor adherence to ART. HRCT chest findings of pulmonary fungal infection were diverse but some characteristic HRCT chest findings were highly suggestive of pulmonary fungal infections in immunocompromised patients. Regular pre ART CD4 cell count every 6 months, early initiation of ART, strict adherence to ART and early diagnosis of treatment failure of ART as per the national ART guideline will be one of the best options for prevention of fungal chest infections.

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# Predisposing Factors of Atrial Fibrillation and Its Association with Left Atrial Dimension: A Cross-sectional Study

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## Abstract

**Background:** Atrial fibrillation (AF) is defined as nonstandard heart rhythm characterized by speedy and asymmetrical beating. Rheumatic heart disease is considered as the foremost reason of AF. Electrocardiography (ECG) and echocardiography (ECHO) are precious noninvasive techniques for quantitatively deciding the size of the left atrium.

**Materials and Methods:** A cross-sectional study was done on 100 patients, who presented with AF. Chest X-ray, ECG, and ECHO of the patients were done and the findings were evaluated.

**Results:** AF was common in patients with mean age of 59.6 years. The male and female ratio in the study was 2:3. The most common etiology of AF was found to be rheumatic heart disease (36%), followed by hypertension (25%), and coronary artery disease (19%). In ECG, 85% of patients with AF showed absent P wave which was the most common finding followed by a variation in R-R interval (72%). Coarse fibrillatory waves (58%) were common than fine (44%). Stage I (41-50 mm) left atrial (LA) dilatation was most common found in AF followed by Stage II (51-60 mm). Stage III was least common presentation.

**Conclusion:** Rheumatic heart disease is the most common underlying etiology of AF in India, and Stage I and Stage II LA dilatation are more prone to develop fibrillation.

**Key words:** Atrial fibrillation, Echocardiography, Electrocardiography, Left atrial dilatation

## INTRODUCTION

Atrial fibrillation (AF) is defined as nonstandard heart rhythm characterized by speedy and asymmetrical beating. Most of the patients are symptomless, but some have complaints of palpitations, dyspnea, chest discomfort, and episodes of fainting. The most common risk factors associated with AF are hypertension, coronary artery disease, valvular heart disease, congenital heart disease, and many others. In developing countries like India, rheumatic fever is usually linked to AF.<sup>1</sup>

AF is a commonly affected heart rhythm and hazardous too. In developed countries such as North America and Europe, the incidence of disease has increased from 0.4-1% in 2005 to 2-3% in 2014. Whereas in developing countries like India about 0.6% males and 0.4% females are affected by this disease. Some studies suggest that incidence of disease also depends on the age group of the patients (0.12% in <50 years age, 5% in 60-70 years of age, and 15% in >80 years of age).<sup>2,3</sup>

The association of AF with a genetic cause has also been established. Four types of mutations in the genes, which leads to disease have been reported. Familial AF is a monogenic disease.<sup>1,4</sup>

AF is also common after cardiac surgeries and in post-myocardial infarction settings but is mostly of limited duration. It is also linked with some non-cardiac circumstances leading to reversible short duration AF such as hyperthyroidism, alcohol consumption, major surgery,

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pulmonary conditions causing hypercapnia. Different studies advocate that condition, which mainly leads to AF, are rheumatic heart disease, coronary artery disease, and hypertension.<sup>4-6</sup>

Most studies favor that rheumatic heart disease is the foremost reason of AF. Some suggest that AF occurs due to the involvement of left atrium by rheumatic fever. Whereas other studies noted that the patients with AF develops left atrium dilatation.<sup>1-8</sup>

Age is also considered as an important feature leading to the progress of AF. Echocardiography (ECHO) is a precious noninvasive technique for quantitatively deciding the size of left atrium.<sup>5</sup>

The current study is done to weigh up the relationship between left atrial (LA) dilatation and presence of AF in patients suffering from different diseases.

## MATERIALS AND METHODS

A cross-sectional study was done on hundred patients who presented with AF from March 2012 to April 2015. Informed consent was taken from all the patients. A detailed history of patients was taken and thorough general and systemic examination was done. Basic investigations, such as hemogram, serum electrolytes, renal function tests, and chest X-ray, were done. All the patients underwent electrocardiography and ECHO.

**Chest X-ray:** X-ray images are used to diagnose the conditions of heart and lung. The PA view of chest was done, and following features were noted:

1. Cardiomegaly
2. LA enlargement
3. Pulmonary congestion.

**Electrocardiogram (ECG):** A 12 lead standard ECG was used in all the patients and features of AF were observed and recorded. If ECG showed irregular baseline, missing P-waves, R-R interval variation and existence of fibrillatory "F" waves were recorded.

**ECHO:** All the patients underwent ECHO. As per the recommendations of American Society of ECHO 2D echo-guided M-mode was used to measure the atrial size. LA enlargement is defined as the measurement of LA dimension more than 40 mm. It also helps in understanding the reason of AF (Table 5).

We graded the LA size according to following criteria:

- Normal (LA dimension <40 mm)
- Stage I (LA dimension 41-50 mm)

- Stage II (LA size 51-60 mm)
- Stage III (LA size >60 mm).

## RESULTS

In this study, the range of age of patients taken under evaluation was 10-90 years with the mean age of 59.6 years. Male and female ratio in the study was 2:3 (males 40, females 60) (Table 1).

Most common etiology of AF in our study was found to be rheumatic heart disease (36%), followed by hypertension (25%), and coronary artery disease (19%). Less common etiological factors for AF were noncardiac (10%) and congenital disorders (7%) (Table 2).

In ECG, 85% of patients with AF showed absent P wave, which was the most common finding followed by a variation in R-R interval (72%). Coarse fibrillatory waves (58%) were common than fine (44%). The more patients showed left ventricular hypertrophy (23%) as compared to left one (21%). Infarction, ischemic changes and axis deviation were also present (Table 3).

In this study, 19% of patients showed no significant findings in chest X-ray. The most common finding was cardiomegaly (72%) and followed by enlarged left atrium (59%) (Table 4).

Stage I (41-50 mm) LA dilatation was most common found in AF followed by Stage II (51-60 mm). Stage III was least common presentation (Figure 1).

**Table 1: Distribution of cases according to age and sex**

Age of patients (years)	n (%)		
	Male patients	Female patients	Total patients
<20	2 (5)	5 (8.3)	7 (7)
20-40	8 (20)	11 (18.3)	19 (19)
40-60	14 (35)	20 (33.3)	34 (34)
60-80	12 (30)	19 (31.6)	31 (31)
>80	4 (10)	5 (8.3)	9 (9)
Total	40 (100)	60 (100)	100 (100)

**Table 2: Diseases associated with AF**

Associated disease	Percentage
Rheumatic heart disease	36
Hypertension	25
Coronary artery disease	19
Congenital heart disease	7
Noncardiac etiology	10
Others	3

AF: Atrial fibrillation

**Table 3: Findings of ECG in patients of AF**

ECG presentation	Percentage
Absent P wave	85
R-R interval variation	72
Fibrillatory waves (coarse)	58
Fibrillatory waves (fine)	44
Left ventricular hypertrophy	23
Right ventricular hypertrophy	21
Infarction changes	9
Ischaemic changes	8
Left axis deviation	9
Right axis deviation	10

ECG: Electrocardiography, AF: Atrial fibrillation

**Table 4: Findings of chest X-ray in patients of AF**

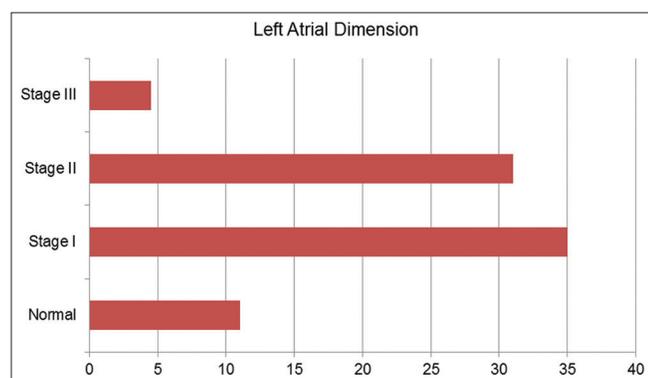
Chest X-ray findings	Percentage
No significant finding	19
Cardiomegaly	72
Enlarged left atrium	59

AF: Atrial fibrillation

**Table 5: Findings of ECHO in patients of AF**

ECHO measurement of left atrium	Percentage
Normal	11
Stage I	35
Stage II	31
Stage III	23

AF: Atrial fibrillation, ECHO: Echocardiography

**Figure 1: Percentage of different dimensions of left atrial enlargement in atrial fibrillation**

## DISCUSSION

According to many studies, the incidence AF was found to be frequent in >45 years of age group. In another study by Arthur *et al.* also supported that AF is more prevalent (89%) in patients >40 years of age. In our study, the mean age of 100 patients who were diagnosed AF was 59.6 years. Supporting many other researches disease was more common in females as compared to males (M: F ratio 2:3).<sup>1</sup>

Regarding etiology of AF, a study by Lévy *et al.* suggested that hypertension (56.4%) is generally the cause of AF.

After that rheumatic heart disease (31%), coronary artery diseases (26.6%), hypertrophic cardiomyopathy (18.5%) were considered as the cause of this disease.<sup>6</sup> Another study advocated that rheumatic heart disease was responsible for AF in 25% of female and 8% of male patients admitted. However in contrast to these researches, rheumatic heart disease (36%) was considered as mainly accountable for AF in our study. Hypertension (25%) was found to be second most common etiology of this disease.<sup>9</sup>

Some studies suggested that the occurrence of AF depends on the size of the left atrium. Cardiac patients with LA dimension below 40 mm were not at risk of AF but those in which the measurements exceeded 40 mm, 54% of patients developed AF.<sup>10</sup> Kulkarni *et al.* recommended that 97.14% rheumatic heart disease patients with LA size of >40 mm developed AF.<sup>7</sup> Similarly, Lévy *et al.* also supported our finding that patients with mean LA size of  $45.8 \pm 8.6$  mm developed AF.<sup>6</sup> Thus, we conclude that there is a strong co-relation between incidence of atrial fibrillation and LA dilatation. If LA size exceeds 40 mm then it is an alarming feature for the patient. Currently, a study conducted by Kulkarni *et al.* in India found that 96.55% patients with LA size of >40 mm (mean = 55.58 mm) progress to develop fibrillation.<sup>7</sup>

Most of the studies support that in ECG (absent P wave and R-R interval variation) and in ECHO (cardiomegaly and enlarged left atrium) are the features which are mostly present in patients with AF.<sup>11-16</sup> The findings of our study are comparable to these results.

## CONCLUSION

AF was frequent in >59 years of age group and is mostly associated with LA enlargement. The most common underlying reason for LA enlargement was rheumatic heart disease, hypertension, coronary artery disease, congenital heart disease. For diagnosis purpose absence of P waves, variation in R-R interval, fine and coarse fibrillatory waves are common findings and in ECHO cardiomegaly and LA dilatation are common features.

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# Profile of Hepatitis B 'e' Antigen and Antibodies to Hepatitis B 'e' Antigen in Hepatitis B Seropositive Patients at a Tertiary Care Hospital in Bengaluru, India

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## Abstract

**Introduction:** Hepatitis B virus (HBV) infection is a disease of global public health significance due to its worldwide distribution and potentially life-threatening sequelae. Prognosis and risk of infectivity is related to the hepatitis B 'e' antigen (HBeAg) status of the infected person.

**Purpose:** In view of the disease burden caused by HBV, the present study was undertaken to assess the seroprevalence of HBeAg and antibody to HBeAg (anti-HBe) in hepatitis B surface antigen (HBsAg) seropositive individuals of both sexes and different age groups.

**Materials and Methods:** A total of 13560 individuals were screened for HBsAg using electrochemiluminescence immunoassay. HBsAg seropositive individuals were further tested for HBeAg and anti-HBe by enzyme-linked immunofluorescent assay.

**Results:** HBsAg was tested positive in 2.12% (287/13560) of the total individuals screened. Out of 287 (179 males and 108 females) HBsAg-positive individuals, 37 (12.89%) were HBeAg-positive, 283 (81.1%) were anti-HBe-positive and 16 (5%) were seronegative for both HBeAg and anti-HBe. Among 37 HBeAg-positives, male to female ratio was 1.3:1 (21:16) with higher seropositivity in individuals aged more than 50 years.

**Conclusion:** HBeAg seroprevalence of 12.89% indicates high infectivity among HBV-infected individuals with higher risk in the advanced age group. The observations in the present study emphasize the need for using various serological markers for diagnosis and screening of HBV infection. Compulsory childhood HBV vaccination programs, massive intervention activities, treatment and awareness programs should be strengthened to control the spread of HBV infection.

**Key words:** Anti-hepatitis B 'e', Chronic hepatitis, Hepatitis B 'e' antigen, Hepatitis B virus

## INTRODUCTION

Hepatitis B virus (HBV) infection is a global health problem and as estimated by the World Health Organization (WHO), approximately 2 billion people have been infected

worldwide, with serological evidence of past or present infection with HBV. More than 350 million (5-7% of the world's population) suffer from chronic HBV infection. Around 15-40% of patients infected with HBV will develop life-threatening liver consequences (including cirrhosis, liver failure, and hepatocellular carcinoma) resulting in 600,000-1.2 million deaths per year due to HBV.<sup>1-3</sup>

In the South-East Asia region, the estimated burden of chronic HBV infection is 100 million. HBV is the second most common cause of acute viral hepatitis after HEV in India. With 3.7% point prevalence, that is, over 40 million HBV carriers, India is considered to have an intermediate

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level of HBV endemicity. Every year, 1 million Indians are at risk for HBV and about 100,000 die from HBV infection.<sup>4</sup> There is no ideal and specific cure for HBV infection. The burden of HBV infection is substantial because of high morbidity and mortality.<sup>5</sup> The silent nature of the disease coupled with significantly untimely death necessitates early, reliable, and affordable method of diagnosis.<sup>6</sup>

The diagnosis, severity and infectivity of HBV infection can be determined by the presence of serological markers such as hepatitis B surface antigen (HBsAg), hepatitis B surface antibody (anti-HBs), hepatitis B core antibody (anti-HBc [IgM and IgG]), hepatitis B envelope antigen (HBeAg), hepatitis B envelope antibody (anti-HBe), and hepatitis B viral DNA (HBV DNA). Though both HBsAg-only - and HBsAg-plus, HBeAg-positive persons are infective to others, additional HBeAg positivity indicates high viral replication and infectivity with HBV DNA levels of  $10^7$ - $10^9$  IU/mL.<sup>7</sup>

The limited data available on the prevalence of HBeAg/anti-HBe positivity among HBV-infected individuals compels the need for determining the presence of HBeAg/anti-HBe, as it signifies the infectivity and prognosis of the HBV infection. Knowledge of the occurrence of HBeAg/anti-HBe seropositivity helps to understand the frequency of highly infective HBV carriers in the given region which in turn helps to design and implement preventive and control measures. Hence, the present study was designed to determine the frequency of HBeAg/anti-HBe seropositivity in hepatitis B individuals in our tertiary care hospital.

## MATERIALS AND METHODS

This hospital based descriptive study was conducted over a period of 26 months (January 2012 to March 2014) at KIMS Hospital and Research Centre a 1000-bedded hospital in Bengaluru, India. A total of 13560 blood samples from patients of all age groups were collected after obtaining the informed oral consent from the patients. Briefly, 2-3 ml of blood was collected from each patient using strict aseptic precautions and serum was obtained using standard methods. The samples were screened for HBV infection by detecting HBsAg in serum by electrochemiluminescence immunoassay using Roche diagnostics Elecsys 2010 immunoassay. HBsAg-negative blood samples were excluded from the study. The samples found to be positive for HBsAg after repeated screening, were further tested for the presence of HBeAg/anti-HBe seropositivity by enzyme-linked immuno fluorescent assay using VIDAS HBe/anti-HBe (BIOMERIEUX, SA France).

HBsAg testing: Roche diagnostics Elecsys 2010 immunoassay was used for detection of HBsAg in serum. Roche diagnostics Elecsys 2010 immunoassay is an automated random access multichannel analyzer for immunological tests intended for *in vitro* quantitation of various analytes including HBsAg. Using electrochemiluminescent technology, the Elecsys HBsAg II test uses biotinylated monoclonal anti-HBsAg antibody and polyclonal anti-HBsAg antibodies labeled with ruthenium complex treated with a serum to form a sandwich. This is attached to streptavidin micro-particles which are electrically initiated to produce chemiluminescence which is read by photomultiplier. Results are obtained automatically by the Elecsys software by comparing the electrochemiluminescence signal obtained from the reaction product of the sample with the signal of the cut-off value previously obtained by HBsAg calibration. Samples with cut-off index  $<0.90$  are non-reactive and those with  $\geq 1.0$  are considered reactive.

### HBeAg/Anti-HBe Testing

VIDAS HBe/anti-HBe (BIOMERIEUX, SA France) was used for qualitative detection of HBeAg and anti-HBe in serum. VIDAS HBe/anti-HBe is an automated qualitative test for use on VIDAS family instruments, for detection of HBe/anti-HBe in serum or plasma by enzyme-linked fluorescent assay technique. All the steps are carried out automatically in the instrument. The solid phase receptacle (SPR) serves as a solid phase. After dilution in the instrument, the sample is cycled in and out of SPR. Meanwhile, the HBeAg present in the sample will bind simultaneously to the specific monoclonal antibody fixed to SPR and to another monoclonal specific antibody conjugated with biotin. The presence of biotin is detected by incubation with streptavidin conjugated with alkaline phosphatase. The conjugate enzyme catalyzes the hydrolysis of the substrate into a fluorescent product, whose fluorescence is measured at 450 nm. The intensity of fluorescence is proportional to the concentration of antigen present in the sample. Results are analyzed automatically.

Descriptive statistical analysis was used for the study to calculate the percentage.

## RESULTS

Out of 13560 individuals tested during the study period, 287 individuals tested positive for HBsAg with a prevalence of 2.12% (Table 1). In the total of 287 HBsAg individuals tested, 179 were males, and 108 were females with the ratio of 1.6:1.

All HBsAg-positive samples were further tested for HBeAg and anti-HBe.

**HBeAg Prevalence**

37/287 samples were positive for HBeAg with the prevalence of 12.89% (Table 2). Out of 37 positives, 21 were male (56.8% cases), and 16 were females (43.2% cases) with the ratio of 1.3:1.

**Anti-HBe Prevalence**

234/287 were seropositive for anti-HBe with a prevalence of 81.5% (Table 2). Out of 234, 148 were males (63.25% cases), and 86 were females (36.75% cases) with a male:female ratio of 1.7:1.

The rate of seropositivity was characterized based on age group, highest HBeAg seroprevalence of 23.52% was found among patients with age >50 years (Figure 1).

**DISCUSSION**

HBV infection with its associated sequel is a disease of major public health importance, being the 10<sup>th</sup> leading cause of death globally.<sup>8</sup> Chronic hepatitis B infection constitutes more than 50% of the chronic hepatitis cases in the India. In milieu of a large population, absence of a compulsory national immunization program and increasing burden of infection and liver disease due to HBV, India may soon have

the largest HBV infection pool in the world, emphasizing the relevance of its HBV epidemiology not only nationally but also internationally.<sup>9</sup>

With the availability of an effective vaccine for over two decades, the national infant immunization program focuses on blocking mother-to-child transmission of hepatitis B with relatively insufficient attention to older age groups, especially adults.<sup>5,9</sup> Vaccine, though available on request, is recommended only for health care workers and other high-risk groups. HBV transmission has become an important health concern among adults, mainly because of difficulties in risk identification and in program implementation.<sup>5</sup>

In contrast to many other viral infections, chronic HBV infection passes through different phases, each of which is in dynamic equilibrium with the other, determined by a closely integrated interaction between the virus and the host immune system.<sup>9</sup> The first asymptomatic immunotolerant phase characterized by seropositivity of HBsAg and HBeAg with high levels of HBV DNA in the serum. The second immunoactive phase, associated with loss of tolerogenic effect, a decrease in HBV DNA concentration, increased ALT levels and increased histologic activity, reflecting immune-mediated lysis of infected hepatocytes. This phase has a variable duration from months to years. The third inactive carrier state phase is of non-replication stage, which occurs after seroconversion from HBeAg positivity to antibody to HBeAg, a marked reduction of serum HBV DNA levels, normal ALT levels and resolution of liver necroinflammation. Inactive HBsAg carriers form the largest group of chronic HBV infected patients. This phase may last for a lifetime. During this stage, HBV DNA may still be detectable by polymerase chain reaction (PCR) in serum and more often in the liver. In rare cases of immunosuppression, as with cancer chemotherapy or after organ transplantation, HBV can be reactivated with the reappearance of HBeAg and high levels of HBV DNA. The patients with inactive HBsAg carrier state may be grouped into three categories (i) HBeAg-positive and anti-HBe-negative, (ii) HBeAg-negative and anti-HBe-positive and (iii) HBeAg and anti-HBe-negative. Majority of our Indian patients belong to the second group.<sup>10</sup>

**Table 1: HBsAg prevalence**

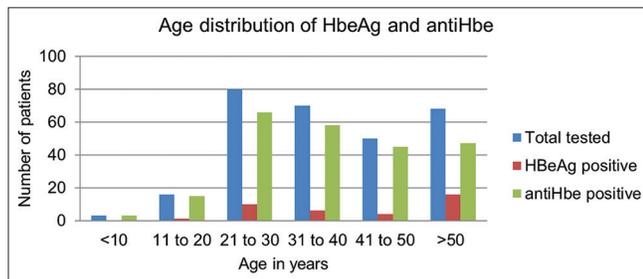
Year	Total tested	HBsAg positive
2012	5310	113
2013	6965	147
2014	1285	27
Total	13560	287

HBsAg: Hepatitis B surface antigen

**Table 2: Seroprevalence of HBeAg and anti-HBe**

Year	HBeAg-positive	Anti-HBe-positive	HBeAg-negative, anti-HBe-negative
2012	14	93	6
2013	16	122	9
2014	7	19	1
Total	37	234	16

HBeAg: Hepatitis B 'e' antigen, HBe: Hepatitis B 'e'



**Figure 1: Age wise distribution of seroprevalence of Hepatitis B 'e' antigen and anti-hepatitis B 'e'**

The present study was performed to assess the seroprevalence of HBeAg/anti-HBe in HBsAg-seropositive individuals in our hospital.

HBsAg is routinely detected qualitatively in HBV infection. HBsAg is also used as a potential marker for monitoring therapeutic responses. Furthermore, the role of serum HBsAg quantification in distinguishing inactive carriers from the subjects having an active form of the disease has also been implicated.<sup>11</sup> The prevalence of HBsAg in

the general population of Asia, Africa, Southern Europe and South America ranges from 2% to 20%.<sup>11</sup> HBsAg seropositivity of 3-4% is reported in the Indian population. There is wide variation in the prevalence in different regions of the country with the highest prevalence in Andaman and Arunachal Pradesh.<sup>9</sup> Various studies across India reports HBsAg seroprevalence ranging from 1.6% to 5.7% in South India,<sup>5,8,12,13</sup> 1.6-3% in North India<sup>14</sup> and 2.97% in West Bengal.<sup>9</sup> HBsAg seropositivity of 2.12% (287/13,560) was observed in our study.

Detection of HBeAg is of little value in typical cases of acute hepatitis. HBeAg usually becomes detectable in the serum when HBsAg first appears but disappears within several weeks as acute hepatitis resolves. However in chronic infection, HBeAg is an important biomarker of viral replication, infectivity and on-going liver injury.<sup>15</sup>

Further analysis of HBsAg-seropositive samples in the present study revealed 12.89% (37/287) positivity for HBeAg with the higher prevalence in males (56.7%) compared to females (43.2%) in the ratio of 1.3:1. HBeAg seropositivity was also found to be high in patients above 50 years of age. The results are consistent with other studies.<sup>8,16</sup> HBeAg seroprevalence of 15-45% has been observed in other studies from south India.<sup>12,13,17</sup> Higher incidence in older age group may be associated with higher prevalence of acute hepatitis in old age. Compared to younger individuals, adults older than 50 years of age are at 1.5 to the twofold higher risk of having chronic HBV infection with the fourfold higher prevalence of HBeAg seropositivity. Furthermore, physiological changes associated with aging, such as diminished immune response ("immune senescence"), metabolic derangements, nutritional deficiencies, and greater cumulative exposure to environmental hepatotoxins may also contribute to worse outcomes of viral hepatitis in the elderly.<sup>18</sup>

In the natural history of HBV infection, the most important event is HBeAg seroconversion characterized by loss of HBeAg and development of antibody to HBeAg (anti-HBe). This generally occurs years after replicative phase and indicates a transition to a low/non-replicative phase with a potential for resolution of infection and improvement of necro-inflammation in the liver. Age of acquisition of the virus, the immune competence of the host and the strength of immune response to the viral antigens are some of the determinants of timing and efficiency of seroconversion. The prognosis of chronic HBV infection is dependent on the amount of inflammation, necrosis and fibrosis in the liver at this point of seroconversion. If the significant liver damage is already present at this point, then the prognosis after seroconversion, spontaneous or treatment related is

unlikely to be good, despite suppression of viral replication. On the other hand, if the seroconversion had occurred early and is maintained, then the long-term prognosis is excellent.<sup>9</sup>

In our study, anti-HBe antibody was found in 81.5% of the study population with higher prevalence in males and patients with age more than 50 years. Several studies have documented 53-90% seroprevalence of anti-HBe antibodies.<sup>17,19,20</sup> We also observed that 5% of HBsAg-positive individuals were seronegative for both HBeAg and anti-HBe antibodies. These patients may be in the early phase of seroconversion.

In a subset of persons, despite anti-HBe positivity, active viral replication persists due to emergence of mutants in the pre-core and basal core promoter regions of HBV. This state, characterized by continuing viral replication despite anti-HBe positivity has been termed as HBeAg-negative hepatitis. Response to anti-viral therapy and outcome of HBeAg-negative hepatitis is different from that of the HBeAg-positive phenotype. It has been increasingly recognized that HBeAg-negative hepatitis is progressively increasing in prevalence globally. In India also, the majority of HBV infected persons are HBeAg-negative, although the exact frequency and prevalence of HBeAg-negative Hepatitis has not been estimated. It would therefore be important to delineate the molecular character, viral load and response to therapy in HBeAg-negative hepatitis in India.<sup>9</sup>

The present work is limited by the scarcity of data regarding the correlation of serological parameters of HBV infection with serum ALT and HBV DNA levels.

## CONCLUSION

The HBsAg seroprevalence of 2.12% was observed in our study of whom 12.89% were seropositive for HBeAg, indicating the presence of highly infective HBV transmission pool among HBV-infected individuals. Hence, testing for various serological markers should be done as a primary test to identify persons with chronic HBV infection. All HBsAg-positive patients who are positive for anti-HBe with elevated ALT levels are considered to be infectious until molecular tests for infectivity like PCR, hybridization for detection of HBV DNA are done to rule out viral core promoter mutant forms of chronic HBeAg-negative viral hepatitis.<sup>6,15</sup> Susceptible adults whose HBV markers are all negative should have repeat test or catch-up immunization, especially those individuals who are in high-risk group.<sup>17,18</sup> Multicenter studies involving the seroprevalence of HBeAg, HBV DNA levels and detection

of viral core promoter mutants are recommended to plan and implement appropriate medical care, vaccination and control strategies.

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# Ultrasonographic Evaluation of Fetal Humerus Length for Assessment of Gestational Age and Its Comparison with Other Conventional Parameters

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## Abstract

**Introduction:** Ultrasonography is proved to be an ideal imaging method, as it is safe for the mother and fetus. It being a painless, non-invasive, non-ionizing, and relatively inexpensive technique used to evaluate fetal growth parameter many times during pregnancy.

**Purpose:** To estimate the gestational age (GA) with humerus length (HL) and establish the accuracy of it as a reliable indicator for prediction of GA in comparison with other routine parameters.

**Materials and Methods:** Prospective study was performed on 100 normal singleton pregnancies at second and third trimesters. The study was conducted on a gray scale real-time ultrasound scanner using linear and sector transducers to measure the fetal biometrics. After visualizing the heart, the transducer is moved to image the scapular spine located on the dorsal surface to the head of the humerus. A straight measurement was made from the one end of the diaphysis to the other.

**Results:** Biparietal diameter (BPD), head circumference (HC), abdominal circumference (AC), and femur length (FL) were compared with standard charts and scatter graphs were plotted. Coefficient of correlation were calculated which were 0.9620, 0.8632, 0.8208, 0.9853 for BPD, HC, AC, and FL, respectively, proving them reliable indicators except for AC. HL measured in the present study was compared with standard nomogram. A statistically significant curvilinear correlation was found between the HL and GA indicating it to be a reliable indicator of GA. Significant coefficient of correlation (0.9704) was observed between HL and GA indicating it to be a reliable parameter.

**Conclusion:** The HL was most accurate parameter next to FL in assessing GA. The study also indicates that combination of BPD, HC, AC, FL, HL is more accurate in predicting GA than any single parameter, particularly in the third trimester of pregnancy. HL would contribute to maximum accuracy next to FL amongst all the parameters.

**Key words:** Femur, Fetal biometry, Gestational age, Humerus, Ultrasonography

## INTRODUCTION

Ultrasound is a safe, non-invasive, non-ionizing, and relatively inexpensive technique for the assessment of obstetric patients.<sup>1,2</sup> Accurate prediction of the gestational

age (GA) is very important in the management of obstetric patients for planning a timely and uneventful outcome. Many antenatal assessment parameters have been studied to predict the correct GA. Biparietal diameter (BPD), head circumference (HC), abdominal circumference (AC) and femur length (FL) are considered reliable predictors and are used as routine parameters. These parameters are helpful in the estimation of fetal age in patients whose fundal height on abdominal examination does not corresponding to the last menstrual period (LMP).<sup>3,4</sup> In cases where the BPD measurement is not reliable femoral length and humeral length allow reliable estimation of fetal age. The purpose of this study is to determine the GA using sonographic

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measurement of the fetal humerus length (HL) and to confirm that it is reliable and essential method in estimation of GA compared with other routine parameters.

## MATERIALS AND METHODS

A prospective study was conducted in the Department of Radio-Diagnosis, MGM Medical College, Indore, Madhya Pradesh, India. The patients were selected from the antenatal clinics, as well as maternity wards. The study was performed on gray scale real time scanner Shimadzu 500 SDU and Shimadzu - Aspire with a 3.5 MHz linear and 3.5 MHz sector transducers. Electronic calipers were used to take measurements. The study envisaged the recording of various routine fetal biometric parameters, as well as fetal HL.

The inclusion criteria included: A history of amenorrhea, confirm date of the 1<sup>st</sup> day of the last normal menstrual period and regular menstrual cycles.

The exclusion criteria were a GA that could not confirmed by early ultrasonography, a discrepancy of more than 10 days between GA by LMP and ultrasound parameter and any malformation.

The patients were between 18 and 35 years of age. 36 out of these were primigravida, and 64 were multigravida; 38 were uniparous, and 23 were multiparous. No patient with a bad obstetric history (i.e., fetal loss more than two in the past) was included in the study.

### Sonographic Procedure

The patients were examined in the supine position exposed from the xiphisternum to the pubic symphysis. The transducer was then placed over the abdomen, and fetal head was identified to ascertain the lie of the fetus, confirm viability and rule out multiple pregnancies.

### Humerus Scanning Technique

After visualizing the heart, the transducer is moved to image the scapular spine which is dorsal to the humerus head. The full length of the humerus was then obtained in a plane as close as possible to right angles of the ultrasound beam. A straight measurement was made from the center of one end of the diaphysis to the other, disregarding any curvature.

### Routine Parameter Scanning

After ascertaining the fetal head position, serial scans were made in a plane transverse to the fetal head. The BPD was measured in a scan that shows the widest diameter at the level of midline echo complex; two lateral ventricle, thalami, and cavum septum pellucidum.

Three measurements were made using freeze frames with electronic calipers. The reference point for BPD is the measurement from the inner margin of distal skull interface to the outer margin of proximal skull interface. The fetal spine was traced from the skull downward till a large anechoic area (fetal bladder) identified anterior to the sacral spine. The transducer was then placed at right angle to mid of heart and bladder to get to the level of AC which was completely circular and included the liver, horizontal portion of portal sinus, as well as the stomach bubble and the fetal spine. The AC was measured with maximum diameter using outer to outer technique. For measuring the FL, the transducer was placed at right angles to the fetal spine and passed down the fetus maintaining this angle to the caudal end. Since the distal femur is usually flexed, the transducer was rotated from this position through 30-45 degrees toward the abdomen until the full length of the femur was visualized. An attempt was made to define both ends of the calcified portion of the femur which was measured when the maximum length was obtained. The HC measurements were taken after obtaining a horizontal section of the fetal head which included both the BPD (corona plane) and the occipitofrontal diameter (sagittal plane). Measurements were taken when the head appeared as an ovoid and echoes from the third ventricle were detected in the midline.

After noting BPD, HC, AC, HL, and FL, the complete information was recorded as in the proforma.

Each parameter was compared with its respective standard chart. The graph was plotted between GA and individual parameters and the accuracy of each parameter evaluated and compared amongst each other.

## RESULTS

A total of 100 pregnant women who were clinically considered to be undergoing an uneventful pregnancy were examined ultrasonographically. In all cases taken up for this study, patients were very sure of the data of their LMP. The GA was calculated from the LMP up to the day of examination with ultrasound, and this was taken as known or standard menstrual age.

The various parameters (BPD, HC, AC, FL, and HL) were meticulously noted.

Each parameter is then compared with its standard chart (western nomograms) and the accurate parameters are noted for that known GA:

- BPD was compared with Sabbagha and Hugheys chart

- HC, AC, and FL were compared with their respective Hadlocks chart
- HL was compared with Jeanty (Western chart).

Fetal maturity was assessed ultrasonographically considering following four conventional parameters:

1. BPD
2. HC
3. AC
4. FL.

Each one of these parameters was independently correlated to GA using standard charts:

- Bi-Parietal diameter (BPD): BPD recorded in the present study was compared with standard nomogram (Sabbagha and Hughey, 1978) (Table 1). It was found that between GA of 16-30 weeks BPD was a good indicator of maturity, except in breech presentation and in dolichocephaly where BPD was not a very good indicator nor it was easily measurable. In the later period of gestation (30-40 weeks), the accuracy of predicting GA by BPD decreases (4-5 mm difference). The maximum error in predicting GA was 4.1 weeks with a mean error of 0.8 weeks. Scatter graph was plotted between BPD and GA, and their correlation was calculated. The overall correlation coefficient between the two was found to be equal to 0.9620.
- HC: HC recorded in the present study was compared with standard nomogram (Table 2). With GA between 16 and 30 weeks, HC was also found to be a good predictor age. Beyond 30 weeks on an average (5-6 mm difference was found between standard and present study data). It was a good parameter when BPD was difficult to detect in cases where the head was in transverse lie or dolichocephaly. The scattered graph was plotted between HC and GA, and their correlation was calculated. Coefficient of correlation was found to be equal to 0.8632 indicating it to be a good parameter for assessing GA. The maximum error in predicting GA was 3.5 weeks with a mean error of 0.93 weeks.
- AC: AC was compared with standard Hadlock chart (Table 3). It was found to be a good predictor of GA in early second trimester, however, in late second trimester and third trimester was found to be an unreliable indicator with maximum error in predicting GA up to 5 weeks and mean error 1.62 week. Nonetheless, it can be used as a predictor of GA in the case in which BPD is technically impossible or in cases in which molding of head can significantly alter the accuracy of BPD. Coefficient of correlation was found to be equal to 0.8208.
- FL: FL correlated well with the standard nomogram (Table 4). Beyond 32 weeks, the FL was 2-3 mm less than standard value. The maximum error in predicting

**Table 1: Comparison of mean BPD in the present study with standard BPD chart**

Gestational age (in weeks)	Standard nomogram (Sabbagha and Hughey) 1978	Mean BPD in present study (in mm)
16	36	36
17	39	40
18	42	40
19	45	44
20	48	47
21	51	51
22	54	53
23	58	56
24	61	60
25	64	62
26	67	67
27	70	69
28	72	70
29	75	74
30	78	76
31	80	78
32	82	80
33	85	81
34	87	83
35	88	85
36	90	86
37	92	88
38	93	89
39	94	90
40	95	90

BPD: Bi-parietal diameter

**Table 2: Comparison of mean HC in the present study with standard HC chart**

Gestational age (weeks)	Standard nomogram (Hadlock <i>et al.</i> , 1982)	Mean HC in present study (mm)
16	122	120
17	134	129
18	148	146
19	160	160
20	177	176
21	182	192
22	193	207
23	208	207
24	221	220
25	239	231
26	241	240
27	256	248
28	271	261
29	273	272
30	276	273
31	281	280
32	292	290
33	302	297
34	308	303
35	317	311
36	322	322
37	328	325
38	334	328
39	340	335
40	345	339

HC: Head circumference

menstrual age was found to be 3 weeks and mean error 0.6 weeks. A highly significant coefficient of

**Table 3: Comparison of mean AC in the present study with standard AC chart**

Gestational age (weeks)	Standard nomogram (Hadlock <i>et al.</i> , 1982)	Mean AC in present study (mm)
16	105	101
17	117	112
18	129	122
19	141	140
20	152	145
21	164	157
22	175	157
23	186	169
24	197	185
25	208	194
26	219	209
27	229	219
28	240	229
29	250	235
30	260	245
31	270	254
32	280	267
33	290	273
34	300	276
35	309	283
36	318	305
37	327	306
38	336	307
39	345	310
40	354	315

AC: Abdominal circumference

**Table 4: Comparison of mean FL in the present study with standard FL chart**

Gestational age (weeks)	Standard nomogram (Hadlock <i>et al.</i> )	Mean FL in present study (mm)
16	23	23
17	26	25
18	28	28
19	30	30
20	33	33
21	35	34
22	38	37
23	40	40
24	42	42
25	45	45
26	47	47
27	49	49
28	52	51
29	54	55
30	57	56
31	59	58
32	61	60
33	64	62
34	66	65
35	69	66
36	71	69
37	73	72
38	76	73
39	78	74
40	80	75

FL: Femur length

correlation (0.9853) between FL and GA was observed indicating it to be a reliable predictor.

**GA Assessment by HL**

HL measured in the present study was compared with standard nomogram suggested by Jeanty (Table 5). The observation showed that present study data correlates well with the standard nomogram throughout gestation. A statistically significant curvilinear correlation was found between the HL and GA indicating it to be a reliable indicator of GA. The sonographic evaluation of humeral length reveals a linear relationship during the second trimester, thus the GA in weeks during this period. However, later in the gestation the growth curve of humerus tends to flatten. The maximum error in predicting GA by HL was found to be 2.3 weeks and mean error 0.71 week. In the majority cases (34%), the HL value were between 50 and 60 mm; corresponding to period of gestation ranging from 30 to 36 weeks (Table 6).

A maximum mean error was found with AC, 1.62 week and least with FL 0.6 week and next to this is HL 0.71 week, indicating it to be reliable predictor of GA (Table 7).

In the majority of cases, the error between humeral age and known menstrual age was between 0 and 1 weeks (Table 8).

Significant coefficient of correlation was observed between HL and GA indicating it to be a reliable parameter (Table 9).

Above observations shows that the HL can be taken as a reliable parameter for recording GA (accuracy 82%) only superseded by FL (accuracy 86%) (Table 10).

**DISCUSSION**

Our observations are self-explanatory, and they are fulfilling almost all the aims and objective for which this study was undertaken. Ultrasonography is a useful means of detecting GA and to monitor fetal growth and development accurately. GA must be reliably established so that needless interference and perinatal mortality rates can be decreased. A total of 100 singleton pregnant women between 16 and 40 weeks of gestational were included in the study. No fetuses with evidence of intrauterine growth retardation, high-risk factors, bad obstetric history were included. The GA was confirmed by clinical examination of the pregnant women at the time of their selection and also if possible from their interrogation on their first visit in an antenatal clinic in early pregnancy. The routing bimanual pelvic examination in the first trimester is a fairly acceptable method of estimating the GA within a range of the 2 weeks.<sup>2</sup>

Patients were excluded if:

1. Their GA, as predicted by the LMP, could not be confirmed by early clinical or ultrasonography examination

**Table 5: Comparison of mean HL in the present study with standard HL chart**

Gestational age (weeks)	Standard nomogram	Mean HL in present study (mm)
16	21	20
17	24	24
18	27	26
19	29	27
20	32	30
21	34	33
22	36	34
23	38	36
24	41	39
25	43	40
26	45	43
27	46	46
28	48	45
29	50	51
30	52	50
31	53	50
32	55	53
33	56	54
34	57	56
35	58	57
36	60	58
37	61	59
38	61	59
39	62	60
40	63	61

**Table 6: Distribution of fetal HL**

Serial number	HL (mm)	Gestational age (weeks)	No of cases	Percentage of cases
1	20-30	16-20	13	13
2	30-40	20-25	18	18
3	40-50	25-30	25	25
4	50-60	30-36	34	34
5	60-70	36-40	10	10
Total			100	100

HL: Humerus length

**Table 7: The error in predicting gestational age with various parameters**

Serial number	Parameters	Maximum error (weeks)	Mean error (weeks)
1	BPD	4.1	0.8
2	HC	3.5	0.93
3	AC	5	1.62
4	FL	3	0.6
5	HL	2.3	0.71

BPD: Bi-parietal diameter, HL: Humerus length, HC: Head circumference, AC: Abdominal circumference FL: Femur length

2. A discrepancy of more than 10 days between the GA predicated by the LMP and that estimated by the ultrasound measurement
3. Impaired fetal growth and malformation existed
4. The patient had any medical complication of pregnancy.

**Table 8: Distribution of error of period of gestation (in weeks) between HL and known menstrual age**

Serial number	Error of gestational age in weeks	Number of cases
1	0-1	93
2	1-2	6
3	2-3	1

HL: Humerus length

**Table 9: Coefficient of correlation between various parameters and GA**

Serial number	Independent variable (x)	Dependent variable (y)	Coefficient of correlation
1	Gestational age	BPD	0.9620
2	Gestational age	HC	0.8632
3	Gestational age	AC	0.8208
4	Gestational age	FL	0.9853
5	Gestational age	HL	0.9704

BPD: Bi-parietal diameter, HL: Humerus length, HC: Head circumference, AC: Abdominal circumference FL: Femur length, GA: Gestational age

**Table 10: Percentage of accuracy of various study parameters in the present study**

Serial number	Parameters	Percentage of accuracy (%)
1	BPD	80
2	HC	75
3	AC	70
4	FL	86
5	HL	82

BPD: Bi-parietal diameter, HL: Humerus length, HC: Head circumference, AC: Abdominal circumference FL: Femur length

Ultrasound is a non-invasive, non-ionizing, inexpensive and safe method of evaluating GA in obstetrical cases. It has been born since 1960s and shall continue to be the same years and ahead. The ultrasound observable parameters currently available are BPD, FL, HC, and AC.

The relationship between the BPD and GA has been studied by various workers.<sup>3,5-7</sup> BPD is a fairly accurate method of estimating the GA.<sup>8</sup> In the present study, the correlation coefficient between GA and BPD is equal to 0.9620, indicating that BPD is highly correlated to GA. However, the natural variations in the growth patterns of the head size in different individuals make the prediction by BPD inaccurate in the third trimester. BPD is also less reliable in breech head, dolichocephaly, uterine anomalies, and multiple gestation. BPD is also difficult to record when the head gets engaged in the late third trimester.

Fetal FL is a relatively easy measurement to obtain. It is especially useful where it is difficult or impossible to obtain a reliable BPD for example, where position or engagement of the head makes visualization difficult or in cases of

hydrocephalus, anencephaly, dolichocephaly where FL can be better relied upon. The FL has a linear relationship with the GA, similar to BPD, but the growth appears to be slow in the third trimester. Fetal FL has been widely used for prediction of GA.<sup>9-12</sup> It has been observed that there is a high degree of positive correlation between GA and FL ( $r = 0.987$ ). In the present study, the correlation coefficient for FL on GA is 0.9853, which is significant. In our study, FL turned out to be a better indicator of GA the BPD, HC, AC, and HL, with percentage accuracy of 86%.

The AC has relationship to GA similar to that of the BPD.<sup>13-16</sup> Because a reproducible AC is more difficult to obtain than a reproducible BPD or FL, this limits its value as a sole estimator of GA. However, these parameters help if other parameters cannot be obtained. The evolution of the variability in predicting menstrual age from AC indicates that it is actually a poor predictor of menstrual age than the BPD except during 36-40 weeks of pregnancy.<sup>15</sup> In the present study, the coefficient of correlation with GA has been found to be 0.8208, indicating 75% of the total variability. The reasons accepted are that the abdomen shape is not constant and is affected by various factors including fetal breathing; in addition certain technical factors may contribute to the fluctuations in the evolution of gestation age by AC. It is a well-documented and established fact that Indian fetal growth does not match with western fetal growth standard due to various socio-economic and environmental factors. In majority of our cases abdominal girth readings were falling short of western standard by 2 SD, but the outcome of fetus after delivery was found to be normal with lower birth weight in comparison with western Hadlock's charts. Hence, they cannot be labeled as case of IUGR in our set up.<sup>17</sup>

HC measurements are acceptable parameters not only for evaluating GA but also in intrauterine growth retardation cases. In situations where the head shape is significantly altered, such as breech presentation or transverse lie, HC measurement offers better correlation than BPD.<sup>16,18-20</sup> HC measurement in our series proves to be a reliable predictor of GA with coefficient of correlation 0.8632. HC correlated well with Hadlock's nomogram up to 30 weeks; after 30 weeks on an average 5-6 mm difference was found between standard western nomograms and present study data. The above observation suggest that a combination of BPD, HC, AC and FL is more accurate in predicting GA than any single parameter particularly in the last trimester of the pregnancy. These conventional parameters were used to confirm the GA of the 100 patients in the present study, to be certain of the GA according to the LMP.

Sonographic measurement of the ossified shaft of fetal humerus is possible after the 12<sup>th</sup> week of gestation.

Humerus is difficult to define accurately, because of its proximity to the chest wall and its apparent continuity with the scapula and clavicle. The relationship between HL and GA has been studied by only few workers. They have stated that HL is also a useful parameter for assessing GA.<sup>21-23</sup> We undertook this study in order to correlate ultrasonographic HL with GA. Various workers have compared linear regression of HL versus GA and demonstrated a strong correlation with " $r = \text{value}$ ." In our present study, the coefficient of correlation was found to be (0.9704) which is highly significant and shows that with increase in GA and HL also increases. Hence, it can be used to assess GA. HL recorded in present study correlated well with the nomograms suggested by Jeanty (1983)<sup>21</sup> with difference of only 2-3 mm in late third trimester. The maximum error in predicting GA with HL was 2.3 weeks, and percentage accuracy of humeral length for assessing GA was 82% which was second most highest than all other conventional parameters. We found that it is a reliable indicator of GA in conjunction with FL, when other parameters do not accurately predict GA. In the management of the patient with premature labor, to accurately predict GA HL can be used in conjunction with BPD and FL. Hence, the present study demonstrates that the ultrasonography measurement of HL is a reliable indicator of GA.

## CONCLUSION

This is a study to assess the HL with ultrasonography in the evaluation of fetal growth and development. The period of gestation was calculated from LMP and clinical examination. With each patient, several biometric parameters were obtained including BPD, HC, AC, FL, and HL.

The mean measurement of these parameters thus obtained for each GA group were compared independently with western nomograms and their accuracy in predicting gest age were determined. The coefficient of correlation of BPD ( $r = 0.9620$ ), FL ( $r = 0.9853$ ), HC ( $r = 0.8632$ ), AC ( $r = 0.8208$ ), and HL ( $r = 0.9704$ ) observed in present study showed a high degree of linear relationship with GA. In our study, AC was found to be an unreliable indicator of GA. It fell short of western standards by  $-2SD$  in the third trimester of pregnancy. This may be because of difference in socio-economic and environmental factors. Therefore, it would be unwise to compare Indian fetal abdominal growth with western standards. A statistical significant positive correlation was found between HL and GA ( $r = 0.9704$ ) indicating it to be reliable predictor of GA. Mean error in predicting GA with HL was only 0.71 week indicating it to be a very accurate parameter. The accuracy of HL was

found to be 82% in predicting GA. Hence, it is a reliable indicator of GA.

The accuracy of various parameters was compared:

- BPD - 80%
- HC - 75%
- FL - 86%
- HL - 82%

It was found that HL was most accurate parameter next to FL in assessing GA.

In condition that may alter shape of fetal skull as well as when abnormality of the BPD and HC is suspected, such as hydrocephalous, anencephaly, breech presentation, multiple gestations, and uterine anomalies. HL can be used as a reliable alternative parameter for estimating GA. In case of preterm labor, in which assessment of several growth parameters help to better approximate GA more accurately, the addition of fetal humerus single length measurement may aid in crucial management decisions. The study also indicates that combination of BPD, HC, AC, FL, HL is more accurate in predicting GA than any single parameter, particularly in the third trimester of pregnancy. HL would contribute to maximum accuracy next to FL amongst all the parameters. It is hoped that sonologists would take up HL also in practice as a parameter for assessing GA in future.

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# Association of Dermal Icterus with Serum Bilirubin in Newborns Weighing <2000 Grams

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## ABSTRACT

**Background:** Neonatal hyperbilirubinemia is a common neonatal problem, with the rise of serum bilirubin there is a corresponding cephalocaudal progression. We are conducting this study to evaluate the strength of association with cephalocaudal progression.

**Objective:** To determine whether the clinical observation is predictable in evaluating the extent of jaundice and then to evaluate the reliability of visual assessment as an indication for the measurement of serum bilirubin level. Whether visual assessment is helpful in the management of jaundiced babies when and where serum bilirubin estimation facilities are not available.

**Materials and Methods:** The study was conducted to find the relation of dermal icterus with serum bilirubin in babies weighing <2000 g. The point of most distal progression of dermal icterus is determined by blanching the skin with the pressure of the thumb and noting the color of underlying skin when the thumb is removed in a well-lighted room.

**Results:** The study was conducted on 100 newborns delivered in the Department of Obstetrics and Gynecology, admitted to Neonatology section of Department of Paediatrics, Government Medical College Patiala. 15 babies had double observation, so a total number of observation was 115. The jaundice was clinically assessed in various dermal zones in natural daylight and total and differential bilirubin was estimated. The statistical analysis comparing serum bilirubin with dermal zones is significant in all dermal zones ( $P < 0.05$ ) except between zones IV and V ( $P > 0.05$ ). The statistical analysis was not significant ( $P > 0.05$ ) comparing male and female newborns.

**Conclusion:** A reliable association is noted between serum bilirubin and cephalocaudal progression of dermal icterus. The association holds true for lower bilirubin (dermal Zones I-III) level, but with the progression of dermal icterus beyond dermal Zone III, serum bilirubin estimation is mandatory.

**Key words:** Encephalopathy, Hyperbilirubinemia, Icterus, Infants

## INTRODUCTION

Neonatal jaundice is the yellow discoloration of the skin and sclera of neonates caused by hyperbilirubinaemia. Bilirubin is a yellow pigment that is produced in the body during the normal recycling of aged red blood cells. About 50% of term and 80% of preterm infants develop jaundice in the 1<sup>st</sup> week of life.<sup>1</sup>

Several risk factors have been identified such as an increased bilirubin load in the hepatocytes as a result of reduced erythrocyte survival, rapid enterohepatic circulation and increased erythrocyte volume. Hyperbilirubinemia is more exaggerated in low birth weight because of the reduced life span of erythrocytes, gastrointestinal immaturity, delayed postnatal maturation of hepatic bilirubin uptake and conjugation. In addition, there is a delay in enteral feeding in sick low birth weight which may lead delay in colonization of intestinal tract of leading to enhancement of bilirubin enterohepatic circulation. These contribute to greater degree and duration of neonatal jaundice in low birth weight babies. Low birth weight and preterm birth are major risk factors for exaggerated hyperbilirubinaemia.<sup>2</sup> clinically significant levels that warrant treatment occur in approximately 50-80% of preterm neonates. Preterm

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infants are at risk of bilirubin encephalopathy at lower total serum bilirubin levels than mature infants.<sup>3</sup>

The increase in total serum bilirubin is accompanied by the progression of dermal icterus from, face to trunks and extremities finally to palms and soles. Hyperbilirubinemia can be safely rule out by eye if jaundice does not reach abdomen or the extremities dermal Zones I and II.<sup>4</sup> The color usually results from accumulation of skin and mucous membranes of unconjugated, nonpolar, lipid soluble bilirubin pigment. Neonatal dermal icterus is not noticeable at serum bilirubin <4 mg/dl.<sup>4</sup>

Pediatrician believes that icterus is a reliable clinical finding among examiners, and its progression and intensity in neonates reflect the degree of rise of serum bilirubin concentration. The cephalocaudal progression was first noted by Kramer in 1969 and found a correlation between the cephalocaudal progression and serum bilirubin with a wide range of bilirubin concentration for jaundice in each dermal zone.<sup>5</sup>

In the present study, we have evaluated the reliability of visual assessment in describing the intensity of jaundice in newborns weighing <2000 g.

## MATERIALS AND METHODS

The study was conducted to correlate dermal icterus with serum bilirubin in newborns weighing <2000 g. The study protocol was approved by the Local Ethical Committee, and parental informed consent was obtained. The study period was from August 2004 to July 2006. The newborns were delivered in the Department of Obstetrics and Gynecology and admitted in a neonatal section of Department of Pediatrics, Government Medical College/Rajindra Hospital, Patiala, Punjab, India. Total and differential serum bilirubin was estimated in Department of Biochemistry. The newborns were randomly selected. The weight of babies was taken at birth. All babies weighing more than 2000 g were excluded from the study. The gestation of newborns ranged from 26 to 41 weeks. The cases were divided arbitrarily into two groups 26-36 weeks (pre-term) and 37-41 weeks as term. Statistical analysis of the cephalocaudal progression of dermal icterus associated with an increase in serum bilirubin was done by using unpaired *t*-test.

Examination of babies was conducted in well-lighted room under natural light. The correct evaluation of dermal icterus is dependent on the amount of lightening. Yellow-white artificial lightening, yellow walls can be extremely misleading. All babies were examined once

every 24 h till baby is placed under phototherapy. The dermal icterus is noted in different dermal zones as shown in Figure 1, dermal Zone I (head and neck), dermal icterus 2 (trunk to umbilicus), dermal Zone III (Groins including upper thighs), dermal Zone IV (knees and elbows to ankles and wrist), dermal Zone V (feet and hands including palms and soles) as shown in Figure 1. The point of most distal progression of dermal icterus is determined by blanching the skin with the pressure of the thumb and noting the color of underlying skin when the thumb is removed. All observations in this study were done by one person, and all bilirubin is processed by one person. Total and serum bilirubin was estimated by Malloy and Evelyn method.<sup>6</sup>

## RESULTS

The study was conducted on 100 Newborns. The jaundice was clinically assessed in various dermal zones in natural daylight from 1<sup>st</sup> day of life. 15 babies had double observations, so a total number of observations was 115. Figure 2 showing serum bilirubin in different dermal zones, out of 115 observations, 4 were made in dermal Zone I; range indirect serum bilirubin was 3.7-5.4 mg/dl with mean of  $4.32 \pm 0.74$ . 32 observations were made in dermal Zone II, with a range of 4.1-11 mg/dl with a mean of  $7.82 \pm 1.59$ . 48 observations were made in dermal Zone III with a range of 6.8-13.5 mg/dl with a mean of  $10.64 \pm 1.18$ . 25 observations were made in dermal Zone IV with a range of 9.2-14 mg/dl with a mean of  $11.47 \pm 1.37$ . 6 observations were made in dermal Zone V with a range of 11.4-20 mg/dl with a mean of  $13.77 \pm 3.17$ .

Table 1 showing statistical analysis of rise of serum bilirubin in different dermal zones which is significant ( $P < 0.001$ ) in all dermal zones except for dermal Zones IV and V where it was not significant ( $P > 0.05$ ). Figure 3 showing comparison between males and females for the rise of serum bilirubin in different dermal zones, after that statistical analysis is shown in Table 2 found no difference in progression of jaundice with serum bilirubin based on gender ( $P > 0.05$ ).

**Table 1: Statistical analysis which was significant in all dermal zones ( $P < 0.05$ ) except in zones IV and V where it was insignificant ( $P > 0.05$ )**

Dermal zones	Unpaired <i>t</i> -test	<i>P</i> value	Significance
II and III	8.54	<0.001	HS
II and IV	9.35	<0.001	HS
II and V	4.50	<0.001	HS
III and IV	2.57	<0.05	S
III and V	2.40	<0.05	S
IV and V	1.75	>0.05	NS

S: Significance, HS: High significance

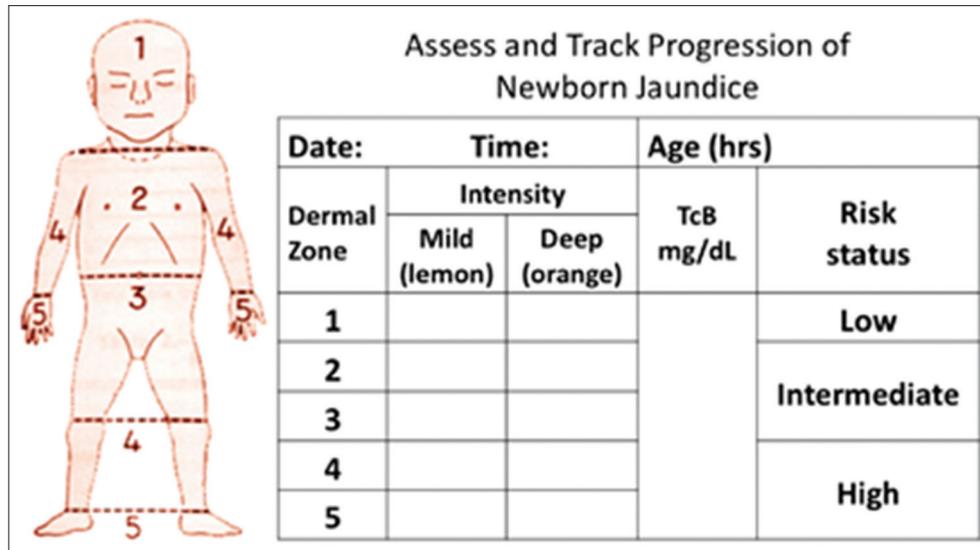


Figure 1: Different dermal zones for assessment of progress of jaundice

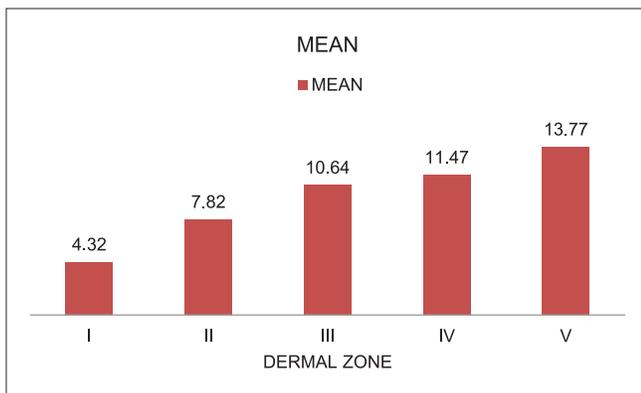


Figure 2: Serum bilirubin in Newborns in different dermal zones

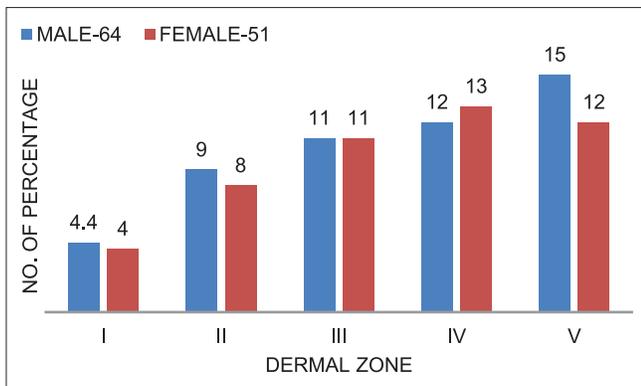


Figure 3: Comparing dermal icterus with serum bilirubin comparing gender

Table 2: Statistical analysis comparing of serum bilirubin in different dermal zone comparing gender

Dermal zones	t-test	P value	Significance
II and III	0.31	>0.05	NS
III and IV	0.21	>0.05	NS
IV and V	1.2	>0.05	NS

S: Significance, HS: High significance

## DISCUSSION

The present study confirms the presence of cephalocaudal progression associated with a rise in serum bilirubin. The American Academy of Pediatrics recommendations for management of hyperbilirubinemia presumes that clinical examination will be sufficient for identification of infants who needs serum bilirubin testing.<sup>7</sup>

In present study serum bilirubin in newborns in different dermal zones is shown in Figure 1, statistical analysis was significant ( $P < 0.05$ ) in dermal Zones I-III but progression beyond dermal Zone III, correlation was not significant ( $P > 0.05$ ). The mean values of indirect serum bilirubin in the present study were different from that reported by Kramer (1969). Kramer made 198 observations of 108 fullterm infants, 82 observations on 40 newborns weighing <2000 g were taken. The comparison of values in present study with that of Kramer has been shown in Table 3.<sup>5</sup>

The present study was in low birth weight babies in which icterus is more easily visible because of immature skin and different bilirubin-albumin binding hence progression of dermal icterus is more rapid as compare to term infants.<sup>8</sup>

Various studies evaluated factors associated with the accumulation of bilirubin in the skin like lipid content of skin, the difference in permeability of albumin in capillaries, local skin perfusion. The cephalocaudal progression is due to conformational changes in newly formed bilirubin albumin complex.<sup>9-11</sup> This conformational change is achieved in 8 s after formation. The reticuloendothelial system (liver and spleen) is site for production of bilirubin hence initial staining

**Table 3: Comparison of rise of bilirubin with cephalocaudal progression of dermal icterus from Kramer with present study**

Dermal zone	Kramer			Present study		
	Number of observation	Range of serum bilirubin	Mean	Number of observation	Range of serum bilirubin	Mean
I	2	4.1-7.5	-	4	3.7-4.2	3.9±0.2
II	14	5.6-12.1	9.49±1.9	28	5.2-11	7.93±1.7
III	8	7.1-14.8	11.4±2.3	37	6.8-12.2	10.76±1.12
IV	24	9.3-18.4	13.3±2.1	21	8-14	11.48±1.46
V	34	>10.5	-	9	11.4-20	13.6±2.9

in central part of body including head and then with increase in bilirubin concentration.<sup>12-14</sup> Bilirubin may be transferred to the skin through two different mechanisms: (1) by leakage of bilirubin-albumin from plasma into extravascular spaces and (2) by precipitation of bilirubin acid in phospholipid membranes. A considerable amount of serum albumin is found outside the blood stream; the extra vascular albumin constitutes about 60% of total in adults. Since bilirubin is bound with albumin and bilirubin-albumin distribution will depend on the distribution of albumin, skin contains a significant amount of albumin hence in cases of hyperbilirubinemia the skin will assume yellow color due to albumin-bilirubin content. Another mechanism is the formation of bilirubin acids when plasma of icteric neonates is saturated with bilirubin acids, the compound to will be precipitated when it will come in contact with phospholipid membrane.<sup>15-17</sup>

Ebbesen also reported caudad progression of icterus corresponds with an increasing bilirubin concentration. The same relationship exists in all infants except in small premature infants in whom it would have been reasonable to measure serum bilirubin when icterus had reached the area below umbilicus (dermal Zone III).<sup>18</sup>

Knudsen *et al.* studied cephalocaudal progression of jaundice in newborns admitted to neonatal intensive care units and confirmed the presence of the same. They found that significant correlation with serum bilirubin in female compared to males. Females have slightly lower albumin concentration than males and the reserve albumin concentration for binding may be slightly low in female, however in present study statistical analysis for correlation of serum bilirubin in different dermal zones showing insignificance ( $P > 0.05$ ).<sup>18</sup>

The present study confirms the correlation of serum bilirubin with the progression of icterus but in low birth weight babies it would have been reasonable to measure serum bilirubin when icterus reaches the area below the umbilicus. Dermal zone assessment is not meant to replace assessment of serum bilirubin it might be helpful in those peripheral hospitals where round clock serum bilirubin

measurement is not available so that early institution of therapy is possible in without waiting for laboratory confirmation.

## CONCLUSION

A reliable association is noted between serum bilirubin and cephalocaudal progression of dermal icterus. The association holds true for lower bilirubin (dermal Zones I-III) level with the rise in bilirubin beyond dermal zone III serum bilirubin estimation is mandatory.

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# An Estimation of Awareness among Practicing Dentists about Proper Ergonomic Practice and its Implications in Delhi - National Capital Region

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## Abstract

**Introduction:** Ergonomics is an applied science concerned with designing products and procedures for maximum efficiency and safety. It is a scientific discipline that studies workers and their relationship to their occupational environment. Dentists and dental hygienists are at more risk for developing work related musculoskeletal disorders (MSDs) as compared to general public. The most frequent injuries occur in spine, back, shoulders, elbows, and hands.

**Objective:** The purpose of this study was to assess the awareness about proper ergonomic practices and its implications among the practicing dentists in Delhi - National Capital Region.

**Results:** Out of 200 clinicians, 178 clinicians (89%) are aware about ergonomics and its implications in the dental office. The majority of clinicians, 115 (57.5%) sometimes and only 16 (8%) always follow proper ergonomics. Statistically, significant results were found in the level of practice of good ergonomics among aware subjects. Analysis of factors contributing to the development of MSDs was also done.

**Conclusion:** There is good awareness about ergonomics among dentists, but the incorporation of the same in their practice is average. Several MSDs have been identified caused due to improper ergonomics. All the subjects were suggested to practice better ergonomics along with several exercises to reduce the progression of MSDs.

**Key words:** Dentistry, Ergonomics, Musculoskeletal disorders, Prolonged static postures

## INTRODUCTION

Just over 1 in 4 of today's 20-year-old will become disabled before they retire.<sup>1</sup> While it is easy to imagine a carpenter falling off a roof or a farmer getting caught in a combine. The reality is many work related injuries occur when the worker is simply sitting in an office chair or a dental stool. In Greek, "Ergo" means work and "Nomos" means natural law or systems. Ergonomics, therefore, is an applied science concerned with designing products and procedures for maximum efficiency and safety.<sup>2</sup> Proper ergonomic design

is necessary to prevent repetitive strain injuries, which can develop over time and lead to long term disability. Ergonomics is concerned with the efficiency of persons in their working environment. It takes account of the worker's capabilities and limitations to ensure that task, equipments, information, and the environment suit each worker.<sup>3</sup> Musculoskeletal disorder (MSD) can affect the body's muscle, joints, tendons, ligaments, and nerves. They are caused by work itself or by working environment. It has been noted that back pain is most common followed by neck pain and shoulder pain.<sup>4</sup> If early signs and symptoms are noted, with the understanding of mechanisms of progression of disease, MSDs can be prevented at a much larger scale. Dental Surgeons are at increased risk of being targeted by the MSDs because of their prolonged working hours and difficult postures. When performing the procedure, dentists try to maintain the neutrality of their posture by exerting undue force on their musculature leading shortening of muscles further progressing to the

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development of MSDs. Their prolonged static postures put them in the dangerous paradox of poor ergonomics which can reflect as chronic low back pain, carpal tunnel syndrome, and cervical spondylitis. Several postures leading to musculoskeletal stresses include:

1. Coordination between the dentist and dental assistant
2. To obtain a clear view of the oral cavity
3. Maneuvering complex armamentarium
4. To provide comfort to the patient during treatment
5. Forceful exertions in tooth extractions
6. Handling of slippery instruments
7. Use of the modified pen grasp in forcefully grasping the instrument with the index finger and the thumb
8. Use of poorly designed small instruments with poor ergonomic grip and blunt edges
9. Prolonged duration of procedures
10. Contact stresses including handling of instruments with narrow grips impinging the bone leading to inflammation and decreased blood flow
11. Psychosocial stresses including time frame crunch and performance anxiety
12. Continuous similar repetitive movements leading to fatigue and stress.

**Objective**

The purpose of this study was to assess the awareness about proper ergonomic practices and its implications among the practicing dentists in Delhi - National Capital Region (NCR).

**METHODOLOGY**

200 practicing dentists in the Delhi - NCR area were randomly selected who voluntarily participated in this study. The collected data were received through self-anonymous - administered questionnaires distributed both in hardcopy and *via* emails from the clinicians on their habits and knowledge about ergonomics. The given questionnaire consisted of 20 questions (Appendix 1) with mostly objective type questions for the ease of operation and less time consumption. Statistical analysis was carried out using the Statistical Package for Social Sciences (SPSS), Version 19.0. Armonk, NY: IBM Corp. Chi-square analysis was used to determine significant differences in data with the *P* value set at 0.05.

**RESULTS**

89% of dentists (178) were aware of proper ergonomics (Table 1), whereas 11% (22) were not aware of ergonomics and its implications in dentistry. 8% (16) claimed that they have never focused on good ergonomics in their practice, and the same amount of dentists claim that they always

follow good ergonomics (Table 2). Statistically, significant results were obtained on analysis of the relationship between subjects aware of ergonomics and their level of practice of ergonomics (Table 3). Analysis of relationship of factors contributing to development of MSDs was done and statistically significant results were obtained with respect to micro breaks in between the procedure, constant vibrations in handpieces, practice four handed dentistry, and the overall physical activity status of the clinician. However, the lighting and temperature of the working are seemed to have no effect in the development of MSDs (Table 4).

**DISCUSSION**

Dentists are one of the highest potential risk professionals for MSDs. The long working hours, difficult postures and high visual demands make the susceptible to the development of MSDs. In our study, 64.5% of the clinicians

**Table 1: Awareness about ergonomics among the subjects**

Response	Frequency (%)
Yes	178 (89)
No	22 (11)
Total	200 (100)

**Table 2: Level of ergonomic practice among the subjects**

Response	Frequency (%)
No response	11 (5.5)
Never	16 (8.0)
Sometimes	115 (57.5)
Every now and then	42 (21)
Always	16 (8.0)
Total	200 (100)

**Table 3: Pearson Chi-square ( $P \leq 0.05$ )**

Value	Df	Asymptotic significance (two-sided)
151.570	4	0.000

**Table 4: Pearson Chi-square ( $P \leq 0.05$ )-Dependent Factor**

Dependent factors	Value	Df	Asymptotic significance (two-sided)
Micro breaks	63.508	4	0.000
Constant vibrations in handpieces	116.706	4	0.000
Temperature of working area	4.257	4	0.372
Lighting of working area	2.770	4	0.597
Four handed dentistry	108.77	2	0.000
Physical activity status	31.081	4	0.000

have experienced symptoms of MSDs during or after performing dental procedures, these statistics correspond with many other studies done on the subject.<sup>5-7</sup> 89% of the subjects showed awareness regarding ergonomics - This was noted as a higher count as compared to the studies done by Kanteshwari *et al.* and Gupta *et al.* which indicated only 50% of the respondents were aware of ergonomics<sup>8,9</sup> and 59.6% in another study done by Gopinadh *et al.*,<sup>10</sup> however despite 89% awareness about ergonomics, only 8% dentists always follow good ergonomic practices in their work. This means more awareness regarding implications of ergonomics in MSDs is required. Several dependent factors were analyzed and the use of micro breaks proved to be useful in reducing fatigue and further injuring the body. Constant vibrations in the handpiece lead to irritation of nerves leading to carpal tunnel syndrome, harmful effects of these vibrations were noted by Åkesson *et al.* (2000) in their study.<sup>11</sup> The practice of four handed dentistry proved to be significant in reducing stress as complimented by Finkbeiner *et al.* (2000, 2001)<sup>12,13</sup> in their studies. Although in a study done by Shetty *et al.* showed that only 27% of the dentists practiced four handed dentistry.<sup>14</sup> The physical activity status of the clinician certainly is an important factor as it affects the strength, endurance, and overall fitness of the body. Surprisingly, the temperature and lighting of the working area seems to have no effect on symptoms of MSDs among the dentists who participated in this study; the results were nonsignificant. However, Lund<sup>15</sup> stresses on optimum temperature and illumination of the working environment for good ergonomics. According to Gupta *et al.* (2014) MSDs also make the primary retiring factor for dentists (29.5%) followed by cardiovascular diseases, neurotic symptoms, etc.<sup>16</sup>

## CONCLUSION

The successful application of ergonomics assures high productivity and avoidance of illnesses and injuries. Unsuccessful application, on the other hand, can lead to

work related MSDs. It is critical to seek prompt medical care for symptoms of ergonomic stress/detect risk factors. We should start incorporating good ergonomics in our dental practice and shall see the results from day 1 in the form of less fatigue and increased efficiency.

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## APPENDIX 1

I.T.S – Centre for Dental Studies and Research, Muradnagar, Ghaziabad

Department of Oral Medicine and Radiology

### ERGONOMIC AWARENESS QUESTIONNAIRE

We are conducting an awareness survey on Ergonomics in Dental Office and would request you to please fill up this short questionnaire. The aim of the survey is to infer the awareness about ergonomics and to identify major risk factors contributing to the development of musculoskeletal disorders due to poor ergonomics.

1. Are you aware of the term 'Ergonomics' and its implications in Dental Office?  
 Yes  
 No
2. If yes, then are you following principles of Ergonomics in your practice?  
 Never  
 Sometimes  
 Every now and then  
 Always
3. Do you take micro breaks (2-5 min) during a procedure?  
 Yes  
 No
4. Are you aware of posture related musculoskeletal disorders?  
 Yes  
 No
5. Have you ever experienced any symptoms in neck, shoulders, hands or back during working?  
 Yes  
 No
6. If yes, please elaborate with duration and intensity of symptoms  

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7. Do you know about any exercises to strengthen your back, shoulders or hands?  
 Yes  
 No

7. If yes, do you practice them?

Yes

No

8. Have you ever noticed that you practice with awkward postures involving excessive bending of the back, prolonged sitting/standing?

Yes

No

9. If yes, Is it a regular practice?

Yes

No

10. Is there constant vibration in the instruments/handpiece you are using?

Yes

No

11. Are you aware of magnification and visualization aids that may help you ergonomically?

Yes

No

12. If yes, do you use them?

Yes

No

13. Is the temperature of the working area comfortable for you?

Yes

No

14. Is the workplace adequately lit?

Yes

No

15. Do you practice four handed dentistry?

Yes

No

16. Did you ever seek medical consult for your symptoms?

Yes

No

17. If yes, did you undergo any treatment?

Yes

No

18. The medical conditions/habits listed below may predispose individuals to repetitive strain injury.

If you have any of the listed conditions and are comfortable disclosing them, please do so.

Rheumatoid arthritis

Diabetes mellitus

Pregnancy

Overweight

Hypothyroidism

Myalgia

Birth control/hormonal drugs

Smoking

Lupus

19. What is your physical activity status? Do you exercise regularly?

Yes

No

This is to certify that the information provided above is true and best of my knowledge

Date:

# Seroprevalence of Human Immunodeficiency Virus, Hepatitis B Virus, Hepatitis C Virus, and Syphilis in Blood Donors at District Level Blood Bank in a Teaching Hospital, Mandya, Karnataka

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## ABSTRACT

**Introduction:** Blood transfusion although saving millions of people worldwide each year, transfusion transmitted infections (TTI) posing a great problem in developing countries such as India. With every unit of blood, there is 1% chance of transfusion-associated problems including transfusion-transmitted diseases. Viral infections cause the major part of mortality and morbidity in blood recipients. According to WHO estimate, the lack of effective screening of blood donors results in up to 16 million new infections with hepatitis B virus (HBV), 5 million new infections with hepatitis C virus (HCV), and 160,000 new cases of human immunodeficiency virus (HIV) infections every year. Screening of the blood donors is, therefore, very essential in preventing TTI's.

**Purpose:** Study aims to know the prevalence of serological markers for HIV, HBV, HCV, and Syphilis among the voluntary and replacement blood donors. Furthermore, to know the high risk age group among the blood donors infected with TTI and their sex distribution.

**Materials and Methods:** After obtaining written consent, all the blood samples collected from donors with sterile aseptic precautions. Blood samples were screened for HIV, HBV, HCV by ELISA, and for syphilis by rapid plasma regain test. All the positive samples were retested by rapid Card method. Any sample found to be positive was discarded.

**Results:** Out of total 14520 blood donors, 12432 (85.6%) were voluntary donors and 2088 (14.4%) were replacement donors. A total of 212 samples found to be positive for TTI. Study demonstrated prevalence of HBV infections as 1.06%, followed by HIV as 0.2%, HCV infections as 0.14%, and Syphilis as 0.05%.

**Conclusion:** The study demonstrated overall seroprevalence of TTI to be low, i.e. 1.4%.

**Key words:** Blood donor, Human immunodeficiency virus infection, Hepatitis B, Hepatitis C, Prevalence, Syphilis, Transfusion

## INTRODUCTION

Blood transfusion history dates back about 200 years. The credit of first successful human to human blood transfusion

goes to Dr. James Blundell, an obstetrician, who successfully transfused 8 oz (227 ml) of blood to a patient of postpartum hemorrhage in 1818.<sup>1</sup> In developing countries, the prevalence of transfusion-transmitted disease is much higher and far from attaining a “zero risk” level at the present moment. With every unit of blood, there is 1% chance of transfusion-associated problems including transfusion-transmitted diseases.<sup>2</sup> Viral infections cause the major part of mortality and morbidity in blood recipients. The majority of known cases of post-transfusion hepatitis has been caused by hepatitis B (HBV) or hepatitis C virus (HCV).<sup>1</sup>

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According to WHO estimate, the lack of effective screening of blood donors' results in up to 16 million new infections with HBV, 5 million new infections with HCV, and 160,000 new cases of HIV infections every year. India is the second most populous nation in the world. The Indian subcontinent is classified as an intermediate HBV endemic (HBs Ag carriage 2-7%) zone and has the second largest global pool of chronic HBV infections. India has a population of more than 1.2 billion with 5.7 (reduced to 2.5) million HIV positive, 43 million HBV positive, and 15 million HCV positive persons.

A recent study by Pahuja *et al.* in 2007, revealed alarming high seroprevalence of HIV, anti-HCV, and HBs Ag (0.56%, 0.6%, and 2.23%, respectively) among blood donors of a metropolitan city like Delhi.<sup>3</sup>

The improved screening and testing of blood donors has significantly reduced transfusion-transmitted diseases in most developed countries. This has not been so in developing nations. Poor health education and lack of awareness result in the reservoir of infections in the population.

Only continuous improvement and implementation of donor selection, sensitive screening tests, and effective inactivation procedures can ensure the elimination or at least reduction of the risk of acquiring transfusion transmitted infections (TTIs).

**Purpose of the Study**

1. To know the prevalence of serological markers for HIV, HBV, HCV, and Syphilis in blood donors in Mandya District
2. To know the high risk age group among the blood donors infected with TTI
3. To know the percentage distribution of male and female sex among positive screened samples.

**MATERIALS AND METHODS**

All apparently healthy adult voluntary donors at blood camps organized by Blood Bank, District Hospital Mandya, Karnataka and replacement donors were taken into the study. Written informed consent was taken. Each donor's name, age, sex, date of birth, permanent address, and contact number were recorded.

A detailed history collected and general physical examination was done. Pulse, blood pressure, Weight, and temperature were recorded for each donor. Any donor with a history of any acute illness in the recent past, tuberculosis, uncontrolled diarrhea, pulmonary disease, recent jaundice, liver disease, cardiovascular disease, and malignancy was noted and excluded.

Any donor with the history of epilepsy, malaria, significant weight loss, unusual, or excessive bleeding and who has recently donated blood within 3 months was excluded. Donors on anti-platelet, anti-epileptic drugs, or anti diabetic drugs were excluded.

Donors below 18 years and above 60 years and women who were menstruating also excluded. Detailed immunization history was also noted. All donors were screened for anemia and for any marks of drug abuse, any skin lesions or active infections at the venipuncture site was also recorded.

Blood was collected with standard aseptic precautions and stored.

A total of 14,520 blood units collected from healthy voluntary and replacement donors during the period from January 2013 to December 2014.

All donor samples were screened for:

- Hepatitis B surface antigen,
- HIV and
- HCV by ELISA, Microlisa-J. Mitra & Co.),
- RPR test for Syphilis by Span Diagnostics Ltd. and
- Malaria by rapid card test (Meriscreen by Meril Diagnostics)
  - All the tests performed according to the manufacturer's guidelines
  - All the reactive samples were repeated in different test with different principle before labeling them seropositive
  - The donated blood discarded whenever the donor sample was found positive for any TTI
  - The statistical analysis was done using the  $\chi^2$  test.

**RESULTS**

Following screening of all blood donors results were Table 1.

Table 1 shows year-wise distribution of voluntary blood donors and replacement donors.

Out of total (14520) blood donors, majority, i.e. 85.6% (12432) were voluntary donors and 14.4% (2088) were replacement donors.

**Table 1: Year-wise distribution of blood donors**

Year	Total blood donors	Voluntary donors (%)	Replacement donors (%)
2013	7398	5908 (79.9)	1490 (20.1)
2014	7122	6524 (91.6)	598 (8.4)
Total	14520	12432 (85.6)	2088 (14.4)

Table 2 shows the distribution of TTI in various age groups. Figure 1 shows distribution of TTI in different age group blood donors.

Of the total 14520 blood samples screened, 212 (1.4%) samples were positive for TTI. Overall percentage was 1.4%.

The majority of donors, i.e. 48 (69.8%) positive samples were from the age group 18-30 years. Next common age group was 31-45 years which were 60 (28.3%). Among both the age groups, hepatitis B infection was predominant.

Figure 2 shows percentage distribution of blood donors by sex. 98% were males, and 2% were females.

Figure 3 shows number-wise distribution of various TTIs in positive samples among blood donors.

Table 3 shows percentage distribution of TTI in voluntary blood donors and replacement donors.

Figure 4 shows percentage prevalence of TTI in voluntary donors

Figure 5 shows percentage distribution of TTI in replacement donors

**Table 2: Age-wise distribution of TTI in blood donors**

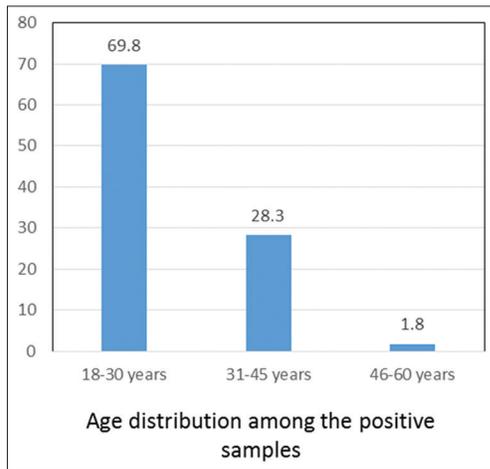
Age group (years)	HIV (%)	HBV (%)	HCV (%)	RPR (%)	Total
18-30	23	108	13	4	148 (69.8)
31-45	6	42	8	4	60 (28.3)
46-60	-	4	-	-	4 (1.8)
Total	29 (13.6)	154 (72.6)	21 (10)	8 (3.8)	212

TTI: Transfusion transmitted infections, HBV: Hepatitis B virus, HCV: Hepatitis C virus, HIV: Human immunodeficiency virus

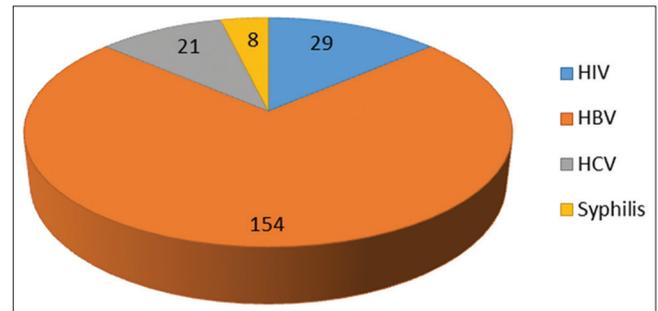
**Table 3: Percentage distribution of TTI in voluntary blood donors and replacement donors**

TTI	Number of voluntary donors (%)	Number of replacement donors (%)	Total (%)
HIV	27 (14.8)	2 (6.9)	29
HBV	129 (70.5)	25 (86.2)	154
HCV	19 (10.4)	2 (6.9)	21
Syphilis	8 (4.3)	0	8
Total	183 (100)	29 (100)	212

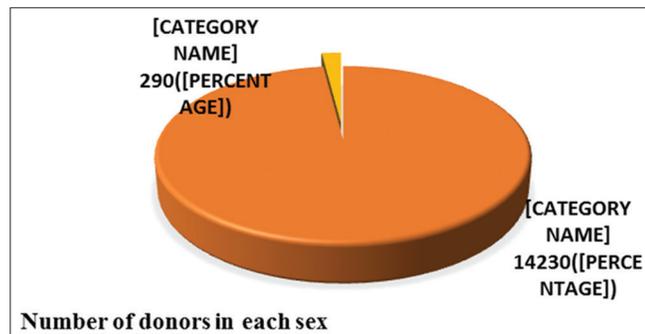
TTI: Transfusion transmitted infections, HBV: Hepatitis B virus, HCV: Hepatitis C virus, HIV: Human immunodeficiency virus



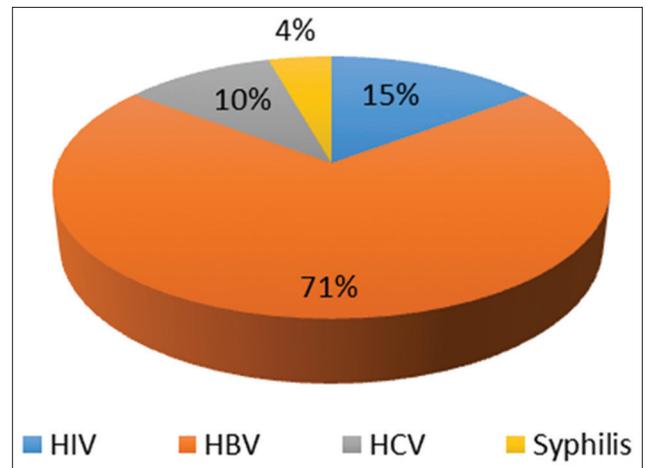
**Figure 1: Percentage distribution positive samples among age groups**



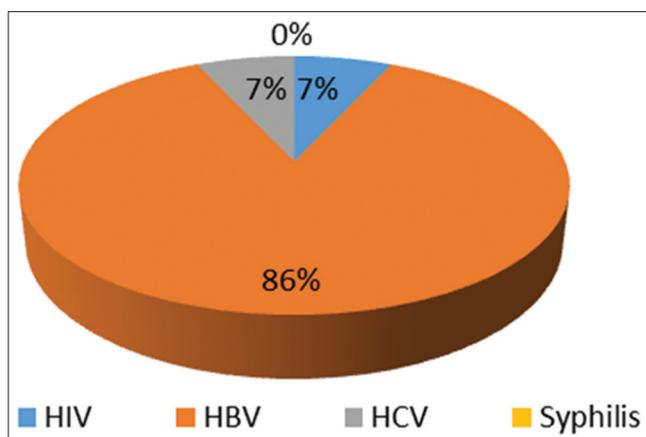
**Figure 3: Distribution of various transfusion transmitted infections in positive samples among blood donors**



**Figure 2: Percentage distribution of blood donors by sex**



**Figure 4: Percentage prevalence of transfusion transmitted infections in voluntary donors**



**Figure 5: Percentage distribution of transfusion transmitted infections in replacement donors**

In our study, the majority of samples were positive for hepatitis B infections 154 (72.6%), followed by HIV infection 29 (13.6%), HCV infections 21 (10%), and Syphilis 8 (3.8%) in that order, out of total 212 positive samples.

In our study, overall prevalence of hepatitis B infections was 1.06%, followed by HIV 0.2%, HCV 0.14%, and Syphilis 0.05%, respectively, out of total 212 positive samples.

Voluntary donors were positive in 183 (86.3%) cases, and replacement donors were positive in 29 (13.7%) cases.

Prevalence of HBV infection was more (86.2%) among replacement donors compared to 70.5% in voluntary donors.

## DISCUSSION

Blood-borne infections are serious problems encountered in blood transfusion. Transfusion related infections have been averted in developed countries by reducing unnecessary transfusions. By using only regular voluntary donors and excluding donors with specific risk factors, this problem can be minimized. Systematic screening of all donated blood for infection also helps in addressing TTI. In contrast, in many developed countries, these interventions are applied uniformly, and the risk of TTI found to be low.

In our study, out of 14520 blood donors, 85.6% (12432) were voluntary donors and 14.4% (2088) were replacement donors, which is similar to the study done by Dr. Shah, *et al.*<sup>4</sup>

We can attribute the increase in voluntary donors to the increasing public awareness and involvement of government bodies like National AIDS Control Organization (NACO) who actively propagate voluntary donation in our country.

However, in a study by Makroo, *et al.*<sup>4</sup> and Arora, *et al.*<sup>5</sup> replacement donors constitute the largest group of blood donors in India, similar findings were reported by other studies.<sup>7-11</sup>

In our study, 98% donors were males, and 2% were females which are similar to other studies. In our study, among the positive samples 69.8% belong to the age group of 18-30 years, and 28.3% belong to 31-45 years age group, which was similar to other studies.

In our study, of the 14520 blood samples screened, 212(1.4%) samples were positive for TTIs, but in a study by Lathamani, *et al.* it was found to be 0.82%.<sup>12</sup>

In our study, the overall prevalence of HBV, HIV, HCV, and Syphilis was 1.06%, 0.2%, 0.14%, and 0.05%, respectively, of total 212 positive samples. Seroprevalence of hepatitis was commonest among the TTI, 70.5% in voluntary and 86.2% in replacement donors.

In a study by Shah, *et al.*, seroprevalence of HIV, HBV, HCV, and syphilis was found to be 0.15%, 0.9%, 0.1%, and 0.2%, respectively. Overall seroprevalence was more in replacement blood donors than that in voluntary blood donors.<sup>4</sup>

In a study in Haryana by Arora, *et al.*, seroprevalence of HIV, HBs Ag, HCV, and syphilis was 0.3%, 1.7%, 1.0%, and 0.9%, respectively. No voluntary donor was found to be HIV positive. The seroprevalence of hepatitis and syphilis were more in replacement donors as compared to voluntary donors.<sup>6</sup>

A study by Singh, *et al.* showed the prevalence of HBs Ag and anti-HCV antibodies was 1.8% and 0.5%, respectively. 83.6% were replacement donors. The prevalence of HBs Ag and anti HCV antibodies ranged between 1.7-2.2% and 0.25-0.9%, respectively, among the donors.<sup>7</sup>

In a study by Pahuja, *et al.*, prevalence of HIV, HBV, and HCV was found to be 0.56%, 2.23%, and 0.66%, respectively. Of all the TTIs, they found a significant decreasing trend for HCV, but not for HIV and HBV infections.<sup>8</sup>

Thakral, *et al.* in her study of seroprevalence of HCV in blood donors, found it to be 0.44%. Interestingly, there was no history of blood transfusion in any of these donors. They concluded that HCV-positive donors should be informed about their disease, counseled and referred to hepatologist, and prevented for future donations permanently.<sup>9</sup>

In their study of HIV infections in blood donors, by Makroo, *et al.* prevalence of HIV was 0.25%. Of the donors

that were tested positive for HIV, 97.4% were males and 2.6% were females. A high rate of HIV positivity, 54.9% was seen in the age group of 18-30 years and 31-40 years age group showed the second highest rate of HIV positives (27.7%).<sup>10</sup>

Lathamani, *et al.* in their study found prevalence of HIV as 0.08%, HBV as 0.5%, HCV as 0.098%, and syphilis as 0.09%.<sup>12</sup>

Garg, *et al.* in their study found prevalence of HIV as 0.44%, HBV as 3.44%, HCV as 0.25%, and syphilis as 0.22%.<sup>13</sup>

Jashim, *et al.* in Bangladesh, found the prevalence of HIV as 0.135%, HBV as 1.4%, HCV as 0.13%, and syphilis as 0.46%.<sup>14</sup>

Bhattacharya, *et al.* in their study found the prevalence of HBV as 1.66%, HIV as 0.35%, HCV as 0.35%, and syphilis as 0.8%. Serious concerns were raised regarding the safety of the blood supply in the community, even after donors were screened for HBs Ag. Transfusion associated HBV infection in India was estimated to be approximately 50% or more in patients who have received a multiple transfusion. They found that in apparently healthy individuals absence of HBs Ag in the blood may not be sufficient to ensure lack of circulating HBV. Blood containing anti-HBc antibodies with or without detectable presence of HBs Ag might be infectious. They suggest that routine anti-HBc screening of blood donations could prevent some transfusion transmitted HBV infections.<sup>15</sup>

The safest blood donors for sustainable blood supply are voluntary, non-remunerated blood donors from low-risk populations. In the key global fact and figures in 2011 (Fact sheet number 279, in 62 countries, national blood supplies are based on 100% or almost 100% (more than 99.9%) voluntary unpaid blood donations. Forty countries collect less than 25% of their blood supplies from voluntary unpaid blood donors. The World Health Organization's (WHO) goal is for all countries to obtain all blood supplies from voluntary unpaid donors by 2020 in accordance with World Health Assembly resolution 28.72, which was adopted in 1975.

World Health Organization and the International Federation of Red Cross and Red Crescent Societies has jointly developed a global framework for action to achieve 100% voluntary blood donation. It is designed to provide guidance and support to countries seeking to establish effective voluntary blood donor programmes, phase out family/replacement blood donation and eliminate paid donation.<sup>16</sup>

Medical history by professional or replacement donors, if concealed pose a great threat to the safe blood supply. Asymptomatic carriers in the society, blood donations during the window period, laboratory errors, and genetic variability in the viral strains also pose problems.<sup>17</sup>

#### Prevention of TTI

- Strategies have been extremely effective, but transmission of diseases still occurs, primarily because of the inability of the test to detect the disease in the “window” phase of their infection
- High cost of screening tests,
- Lack of funds and trained laboratory personnel,
- Genetically variant viruses,
- Non-seroconverting immune silent or chronic carriers and
- Laboratory testing errors.

#### CONCLUSION

Out of 14520 healthy donor samples, 212 cases screened positive. The overall prevalence of TTI's was 1.4%. Voluntary donors forms the majority 85.6% in our study; that shows good awareness among the population. In our study, overall prevalence of HBC, HIV, HCV, and Syphilis was 1.06%, 0.2%, 0.14%, and 0.05% respectively. Among the TTI, HBV was the more common in both voluntary and replacement donors, 70.5% and 86.2%, respectively. Among the positives samples, 98% were males and 2% were females, highest 69.8% were between 18 and 30 years, the second highest 28.3 % were from 31 to 45 age group. Study proves that many apparently healthy blood donors are not safe donors, so extensive donor selection and screening is mandatory. The present study concludes that motivating voluntary blood donors are the most effective way of ensuring adequate supplies of safe blood on a continuing basis.

#### Recommendations

- To reduce the risk of these infections non-remunerated repeat voluntary donor services need to be instituted
- The emphasis must also be laid on voluntary risk reduction, which will require increased awareness and change in the attitude of people
- Sterile aseptic precautions should be followed by medical staff while collecting and performing tests.

Even though the seroprevalence of blood borne infection is low among voluntary blood donors in Mandya, a larger study to generate more accurate estimates of the magnitude of the TTI diseases would be needed. Thus, understanding the demographic data would still reduce the overall burden on health care system.

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# Utilization of Social Security Schemes among Elderly in Kannamangala, Bengaluru

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## Abstract

**Introduction:** In India, 8% of total population constitute elderly people among which 69% reside in rural area & half of them were Below Poverty Line (BPL), for whom Govt projected Social security schemes. But utilization of these schemes is questionable, so the present study is conducted to know the level of utilization of these schemes.

**Objectives:** a) To understand the awareness regarding existing social security schemes among elderly and other family members. b) To know the pattern of utilization of these schemes. c) To list the challenges faced by elderly in utilizing these schemes.

**Methodology:** Descriptive study carried out in the Field practice area of Vydehi Institute of Medical Sciences and Research Centre, Bangalore. A total of 244 elderly patients (60 years old and above) were interviewed using a pre-tested semi-structure questionnaire including socio-demographic profile of elderly. Findings were described in terms of proportions and percentages to study awareness, utilization and challenges faced in utilizing the social security schemes.

**RESULTS:** Around 48.5% were in the age group 60-69 years, more than half (82%) were illiterate and nearly 92% were below poverty line. 49.5% of elderly and 32% of their family members are aware of security schemes. Maximum (66.6%) utilization was for social assistance schemes and were mainly (56.6%) used for basic needs. 79.5% people complains of insufficiency of fund to meet their basic needs.

**Conclusion:** Study results showed that there is need for increase in funds to meet basic needs of an elderly and also for Information, Education and Communication (IEC) to increase awareness and utilization of schemes.

**Key words:** Elderly, Social security, Utilization

## INTRODUCTION

As the life expectancy is rising, the population of the aged people is also increasing steadily. This demographic change resulted in change in structure of the population. In 2010, 8% of the world's population constituted population. This is expected to increase to 19% by 2050.<sup>1</sup> In India, 8% of total population constitute elderly people among whom 69% reside in the rural area and half of them are below poverty line (BPL).

Ageing is a development issue and healthy older persons are a resource for all who make major contributions to the society. The Government of India realized this and projected a social and income security in the year 1999 which plays an important role in poverty alleviation and healthy life of the elderly.<sup>2</sup>

The gradual collapse of the traditional old age support mechanism and rise in elderly population highlighted the need for appropriate formal channels.<sup>3</sup> The reducing family support increases the responsibility of the state to ensure the welfare of older persons.

Social security is a safeguard mechanism, which a society extends to its fellow members to warrant income security and attainability of the welfare services, especially for the vulnerable sections of the society.<sup>4</sup>

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International Labor Organization (2006) defines social security as “the set of institutions, measures, rights and obligations whose primary goal is to provide income security and medical care to individual members of the society.”<sup>5</sup> It is a social wellbeing and system that ensure this. In simple terms, the signatories agree that society in which a person lives should help them to develop and to make the most of all advantages (culture, work, social welfare) which are offered to them in the country.

Unlike other countries in the United States, India does not have a Universal Pension System. There are no comprehensive social security schemes as a whole (Rajan and Liebig, 2003).<sup>6</sup> Adopted pension policy is restricted to workers in organized sectors leaving out 90% of workers in unorganized sectors.<sup>7</sup>

Though the policy holders raised the problem of state's affordability in providing social security benefits to growing elderly population, how far these schemes are efficient in providing support and how far it has been used properly by elderly is a matter of concern. The present study was taken up based on the following objectives:

- To understand the awareness regarding existing social security schemes among elderly and other family members
- To know the pattern of utilization of these schemes
- To list the challenges faced by elderly in utilizing these schemes.

## METHODOLOGY

A community based cross-sectional study was carried out for 1 month from July to August 2014. The study subjects included were elderly men and women aged 60 years and above who belonged to rural field practice area of Vydehi Institute of Medical Sciences and Research Centre, Bengaluru, Karnataka, India.

The field practice area consists of four villages - Kannamangala, Dhinnur, Bevinamara Colony and Jyothi Bapule Nagar with a population of 4764, there were 244 (5.2%) elderly people in these villages.

A pretested semi-structured questionnaire was distributed to 210 elderly peoples willing to participate in the study. The purpose of the study was explained to them and oral informed consent was obtained. Care was taken to ensure privacy and confidentiality. Sometimes they were called separately and interviewed where he/she could feel comfortable to avoid interference and influence of other family members and neighbors.

**Table 1: Demographic distribution of the respondents**

Demographic details	Males n=92 (%)	Females n=118 (%)	Total n=210 (%)
Age			
60-69	45 (48.9)	57 (48.3)	102 (48.5)
70-79	32 (34.7)	53 (44.9)	85 (40.4)
80-89	13 (14.1)	17 (14.4)	30 (14.2)
90 and above	02 (2.1)	01 (0.84)	03 (1.42)
Marital status			
Married	67 (72.8)	45 (38.1)	112 (53.3)
Single	3 (3.2)	1 (0.84)	4 (1.9)
Separated	00	4 (3.38)	4 (1.9)
Widow/widower	22 (23.9)	68 (57.6)	90 (42.8)
Education			
Illiterate	76 (82.6)	104 (88.13)	172 (81.9)
Primary	11 (11.9)	12 (10.16)	29 (13.8)
secondary	5 (5.4)	2 (1.6)	9 (4.2)
Socioeconomic status			
BPL	84 (91.3)	109 (92.3)	193 (91.9)
APL	8 (8.6)	9 (7.6)	19 (9.04)
Source of income			
Pension	53 (57.6)	48 (40.6)	101 (48.0)
From children	13 (14.1)	26 (22.00)	39 (18.57)
Borrowing from relatives/friends	10 (10.8)	21 (17.7)	31 (14.7)
Self-employment	52(56.5)	24(20.3)	76(36.1)
Occupation			
Agriculture	64 (63.3)	37 (36.6)	101(48)
Labor	42 (62.6)	25 (37.3)	67 (32)
Non-workers	29 (69.0)	13 (30.9)	42 (20)

BPL: Below poverty line, APL: Above poverty line

**Table 2: Awareness regarding social security schemes**

Awareness of Schemes	Male (%)	Female (%)	Total (%)
Respondents			
Yes	62 (67.3)	42 (36.4)	104 (49.5)
No	30 (32.6)	56 (47.4)	106 (50.5)
Family members			
Spouse	23 (25.0)	44 (37.2)	67 (31.9)
In-laws	68 (73.9)	72 (61.0)	140 (66.6)
Children	81 (88.0)	87 (73.7)	168 (80.0)
Others	26 (28.2)	21 (17.7)	98 (46.6)
Source of awareness			
Local leaders/panchayat	10 (10.8)	14 (11.8)	24 (11.4)
Voluntary agencies	46 (50.0)	52 (44.06)	108 (51.4)
Children	34 (36.9)	28 (23.7)	64 (30.4)
Relatives/friends	62 (67.2)	46 (38.9)	108 (51.4)
Media	2 (2.17)	4 (3.38)	6 (2.85)

The data collected was entered into an Excel sheet and analyzed using statistical package SPSS version 21. The findings were described using proportions and percentages.

## RESULTS

The socio-demographic characteristics are depicted in Table 1.

**Table 3: Utilization pattern of social security schemes**

Utilization of schemes	Males (%)	Females (%)	Total (%)
<b>Social security schemes</b>			
Social assistance schemes	72 (78.2)	68 (57.6)	140 (66.6)
Pension schemes	53 (57.6)	48 (40.6)	101 (48.0)
Social security benefits	54 (58.6)	46 (38.9)	100 (47.6)
Free medical services	22 (23.9)	34 (28.8)	56 (26.6)
Tax rebate	30 (32.6)	19 (16.1)	49 (23.3)
Travel concession	21 (22.8)	26 (22.03)	47 (22.3)
Insurance	18 (19.5)	11 (9.3)	29 (13.8)
Other benefits	12 (13.04)	09 (7.6)	21 (10.00)
<b>Purpose of utilization</b>			
Basic needs	58 (63.00)	61 (51.6)	119 (56.6)
Health care and medicines	16 (17.39)	14 (11.8)	30 (14.2)
Give to children/spouse	7 (7.6)	31 (26.2)	38 (18.09)
Loan payments	3 (3.2)	00	3 (1.4)
Own needs	8 (8.6)	10 (8.4)	18 (8.5)
Others (habits)	2 (2.17)	00	2 (0.95)
<b>People helped in availing schemes</b>			
Children	43 (46.7)	86 (72.8)	129 (61.4)
Relatives	26 (28.2)	16 (13.5)	42 (20.00)
Friends	3 (3.2)	14 (11.8)	17 (8.09)
Others (NGO's, neighbors)	00	2 (1.6)	2 (0.95)
<b>Sufficiency of amount</b>			
Enough to meet basic needs	12 (13.01)	6 (5.08)	18 (8.5)
Sometimes found difficult to meet basic needs	11 (11.9)	14 (11.8)	25 (11.9)
Not sufficient to meet basic needs	69 (75.0)	98 (83.0)	167 (79.5)

The study revealed that there were 102 (48.5%) persons who were young old, 85 (40.4%) old and 33 (15.6%) oldest old in the area. 53.3% of them were married. It was seen that 172 (81.9%) were illiterate and only 9 (4.2%) had received secondary school education. Nearly 193 (92%) were BPL. Majority of them, 168 (80%) continues to work, among which 67 (32%) as laborers and 101 (48%) works in agriculture. National pension forms the major source of income for 101 (48%) of elderly.

The awareness of the various social security schemes is depicted in Table 2. The study showed that 104 (49.5%) of the elderly, 67 (31.9%) of the family members were aware of schemes. Voluntary agencies and relatives or friends were the main source of information.

It can be seen from Table 3 that maximum utilization 140 (66.6%) was for social assistance schemes and least 29 (13.8%) was for insurance. The funds were mainly used for basic needs by 56.6% of the elderly. However, it was noted that 14.2% of elderly utilized the money for medicine and 18.1% even gave it to their children and spouse. In majority 129 (61.4%) the children of elderly helped in availing the schemes.

The fund amount was not sufficient to meet the basic needs of food, clothing and shelter in 167 (79.5%) of them.

Challenges faced in utilization of schemes is mainly due to lack of awareness that is 86 (40.9%) elderly people were unaware of schemes, followed by physical constraints about 67 (31.9%), used by their children 62 (29.5%), lack of knowledge 54 (25.7%), transport 31 (14.7%), not accessible 25 (11.9%) and not fit in eligibility criteria 19 (9%).

## DISCUSSION

Major fraction 102 (48.5%) of elderly population was in the age group of 60-69 years, while small fraction of 33 (15%) were 80 years above. Lena *et al.*<sup>8</sup> showed in their study conducted at Udipi Taluk as 72% of population were ranging from 60 to 69 years old and 3% were above 80 years old.

Padda *et al.*<sup>9</sup> reported 36.6% illiteracy at Amritsar, while it was 78% in Tamil Nadu by Elango<sup>10</sup> and Singh *et al.*<sup>11</sup> reported 80.2% as compared to this study where illiteracy is about 172 (81.9%). The proportion of elderly married, widowed, or unmarried were found to be similar to the study conducted by Singh *et al.* and Shah<sup>12</sup> reports that 64.3% of elderly women were widows when compared to this study is 90 (42.8%).

This study, showed that 168 (80%) were still working as unskilled workers (agriculture and laborers). Similar results were seen in a study done by Elango while Singh *et al.* reported that 55.8% were occupied in productive work, 28% in agriculture, 15.1% in labor, and 44.2% were dependent on others.

Goel *et al.*<sup>13</sup> showed 46.3% elderly were not aware of any geriatric welfare services and 96% of them had never utilized any services as compared to this study it is 140 (66.6%). Sanyal<sup>14</sup> showed in his paperwork that, overall utilization of beneficiary schemes by elderly is about 42.4% whereas in this study is 100 (47.6%).

Gaya<sup>15</sup> written that inadequacy of benefits, delays in payments, lack of up to date information about the schemes and the amount of individual contributions made and estimated benefits were the challenges faced for utilization of schemes in Tanzania and Tostensen<sup>16</sup> mentioned that the governance and management of public social security institutions including the deficiencies in record keeping and the processing of benefit claims are the challenges mainly faced in Africa whereas in this study, lack of awareness of social security schemes followed by physical constraints are main challenges.

## CONCLUSION

77% of males and 50% of females are utilizing some form of social security schemes. 53% of elderly find it difficulty

in utilizing the social security schemes and 79% found it's not sufficient to meet their basic needs.

Majority of elderly are illiterate (82%), BPL (92%), and are partially or totally dependent on others for their economic needs. So, there is a growing need for interventions to ensure income security for this vulnerable group and to create a policy to meet their needs which can be achieved by strengthening the social and political support at different levels.

Social security is the major source of income in 48% of elderly. However its adequacy, affordability and sustainability are still questionable and in draw attention to raise the social security benefits to the elderly in the rural.

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# Quiz versus Didactic Lecture on Undergraduate Students of BJ Medical College, Ahmedabad: A Cross-Sectional, Comparative, and Interventional Study

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## Abstract

**Introduction:** The vision 2015 document published by Medical Council of India expressed the policies and strategies of Government of India regarding medical education in coming years. There is an association between the methods used in lecture to deliver the contents and the knowledge gain by students. A surface learning suggests only superficial knowledge without understanding, but deep learning is means to be acquired skills to analyzed, synthesize, and cognitive skills to derive conclusion pertain to subject.

**Methodology:** The study was a cross-sectional, comparative, and interventional. The quiz on swine flu to enhance participation and interest of the students conducted in the seventh semester (III/I) during the month of February 2015 in the Department of Community Medicine, BJ Medical College, and Ahmedabad as an alternative to the conventional lecture (Topic-Reproductive and Child Health Services). The students were given notice 2 weeks prior for the preparation.

**Results:** In the pre-test, the majority of the students 57 (63%) scored <40%. Another 29 students (32%) had scores between 41% and 60%. In the post-test evaluation, 41 (46%) obtained 81-100% followed by 32 (35.55%) and the rest 17 (19%) below 40% score. The winning teams both Team B and Team A scored 75% and 55%, respectively.

**Conclusion:** There was an exceptional improvement in students' performance in post-test analysis of swine flu quiz, as compared to the didactic lecture on mother and child health. It was possible to adopt interactive teaching as a method in conventional curriculum despite associated challenges. So, instead of subjecting students to the lectures, we can use different interactive teaching methods to incorporate in the schedule to give them better insight on the subject and to save energy and time.

**Key words:** Comparative, Didactic lecture, Quiz, Swine flu

## INTRODUCTION

The medical council of India published the policies and strategies of medical education every year with the objective to improve quality and standards of medical education and training. It is also to make an Indian graduate medical

doctor skilled to maintain the standards in graduation complied according to strategies mentioned in vision 2015.<sup>1</sup>

Teaching and learning are the two important components of education. So, there were considerable changes in the education system at the medical workplace because of strong correlation between the methods used in delivering the information by the lecturers and the assimilation of that knowledge by the students. So we can change the way for teaching and learning the process in a better way to both how and what is taught. "Deep learning"<sup>2</sup> requires higher order cognitive skills such as analysis and synthesis, while "surface learning consists primarily of comprehension and reproducing knowledge." This requires the acquisition of

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four main domains of competencies defined by the Medical Council<sup>3</sup> as: (1) Knowledge, skills, and performance; (2) safety and quality; (3) communication, partnership, and teamwork; and (4) maintaining trust.

The MCI Vision 2015 states that lectures are not adequate as a method of teaching and training also a poor method of transferring or acquiring information.<sup>4</sup> The lectures have less impact at skill development and attitudes and competence-based education, and we encountered large classes, for example, 120 approximate per class. So, there is need of innovation in the form of active learning oppose to passive learning.<sup>5</sup>

The didactic lectures have certain drawbacks such as loss of interest or limited attention span, less retention of subject, passive learning. There is lack of development of any logical or analytical skills because the students are only listening and not actively participating during lecture. There is no active interaction or feedback from the students.<sup>6,7</sup>

The purpose of interactive teaching methods are generation of interest in the subject and acquirement of more knowledge in general, active and participatory learning, development of life-long learning habits and attitudes, acquire, retain and apply the knowledge, active involvement of students, thorough understanding of the subject, use of internet and other options at disposal for better understanding of matter, promote group learning, heightened motivation, and enthusiasm.<sup>8</sup> Active listening of opinions of others and asking questions.

The main purpose of the quiz competition was to introduce the scope of the subject to medical students and obtain their feedback on its conduct and utility as a teaching and learning method.

### Aims and Objectives

1. To ascertain the effectiveness of quiz as an interactive teaching technique in lectures
2. To implement various quizzing activities in lectures and evaluate their impact on learning.

### METHODOLOGY

This was a cross-sectional, comparative, and Interventional study. The quiz as a mode to enhance participation and interest was conducted for students studying in seventh semester (III/I) during the month of February 2015 in the Department of Community Medicine, BJ Medical College, and Ahmedabad as an alternative to the conventional lecture of Reproductive and Child Health (RCH) Services. The topic and schedule of the quiz was announced 2 weeks

in advance. Time frame and work schedule were mentioned according to grant chart. Figure 1 shows the flowchart for conduction of the quiz on swine flu. The collected data was fed using the statistical package using Microsoft Excel and analyzed.

The assessment tools for data collection was predesigned feedback questionnaire from students and for faculty as an observer's perception, pre- and post-test questionnaire - for didactic lecture, score system of multiple choice question (MCQ), short answer question and other rapid fire rounds of the quiz also power point presentations and videography to conduct quiz rounds, scores of pre- post-session MCQ tests for quiz. The questionnaire with a five point Likert's scale was also used where (5) was suggest very important/very good, and (1) represented least important/very poor, used as innovation in teaching-learning method, students and faculty perception in pre-tested and predesigned questionnaire.

### RESULTS

There were 121 students enrolled in the X batch, among them 82 (68%) students attended the didactic lecture on "RCH" while out of 121 students in Y batch, 90 (75%) students attended quiz on "swine flu outbreak." In total, this quiz was attended by 90 MBBS students, 30 residents of community medicine, 9 tutors, 4 APs, 2 associate professors, and 2 professors. All the 7 competencies viz. history taking, physical examination, data assessment, therapeutic management, doctor-patient relationship, professional behavior and work ethics, and oral presentations and written documentation for mini-CEX, were observed.

Table 1 shows that following aspects had covered in six rounds. They were concepts of disease, determinants related to health; genetic factors, lifestyle factors, environmental factors round, epidemiology and screening, preventive medicine, hospital case management, epidemic control, and health education of disease.

Table 2 gives the winning team and their score. The overall performance was encouraging. The winning teams both Team B and Team A scored 75% and 55%, respectively.

Table 3 gives the evaluation of students by pre-test and post-test. In the pre-test, the majority of the students 47 (52%) scored <40%. Another 29 students (36%) had scores between 41% and 60%. In the post-test evaluation, 41 (46%) obtained 81-100% followed by 32 (35.55%) and the rest 17 (19%) below 40% score. The difference between pre-test and post-test scores was found to be statistically

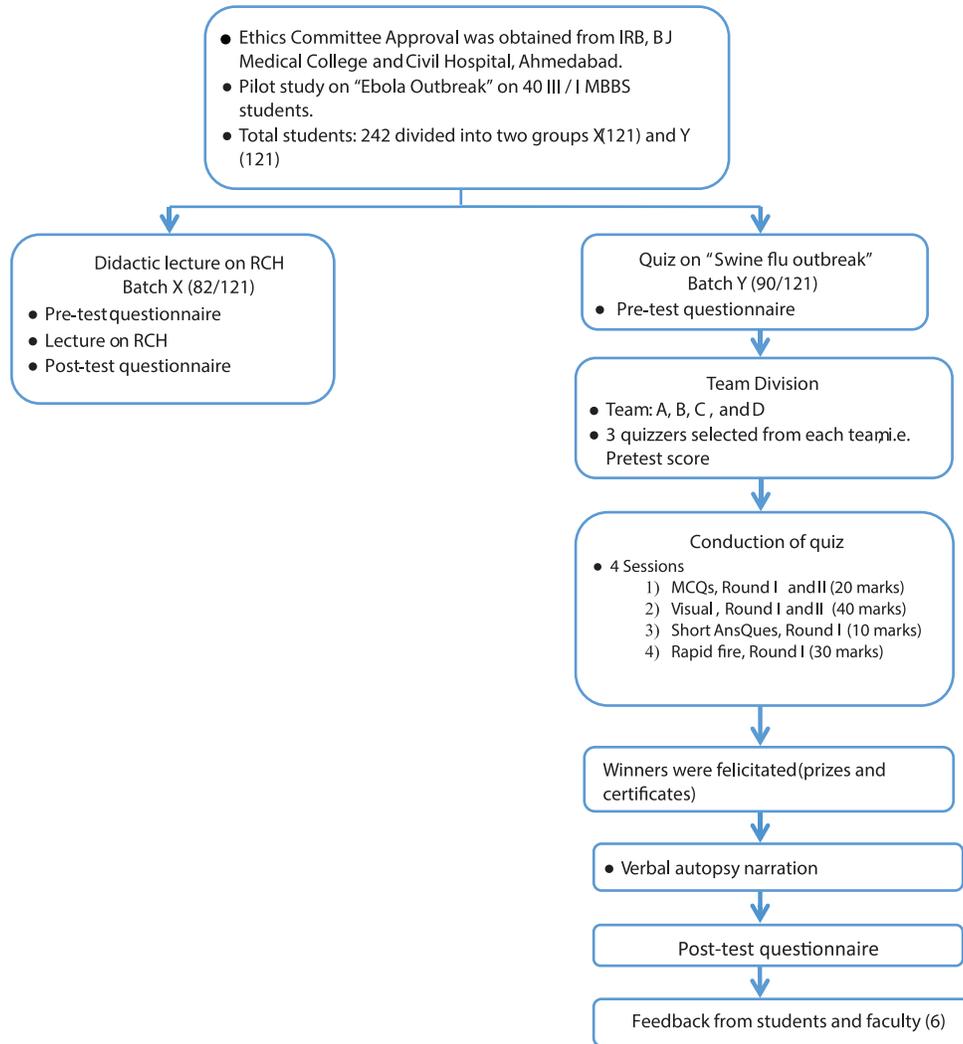


Figure 1: Flowchart for conduction of quiz on swine flu

Table 1: Details of contents of each round, time allotment, maximum marks, and examples

Category	Time	Marks	Examples
Session 1: MCQ round	1 min for each question	Two rounds with 10 marks each (max marks=20)	What is the period for swine flu vaccine to activate in a person's body? (1) 2 h, (2) 3 weeks, (3) 15 days, (4) 1 month
Session 2: Visual round	2 min for each question	Two rounds with 20 marks each (max marks=40)	Identify the district of Gujarat where maximum swine flu cases occurred during recent pandemic. Give account of total death and positive cases in that district?
Session 3: Short answer round	1 min for each question	One round with 10 marks each (max marks=10)	(1) Ahmedabad, (2) Jamnagar, (3) Rajkot, (4) Kutch Describe infection control measures at individual level and health facility level
Session 4: Rapid fire round	30 s for all questions	One round with 3 questions each carrying 10 marks (max marks=30)	Describe the antigenic shift, antigenic drift and the difference in all pandemics of swine flu till today

MCQ: Multiple choice question

highly significant. It also shows that previously it was 33% students had scores between 41% and 60% which converted into 49% in post-test lecture. There was an exceptional improvement in performance in the post-test analysis of swine flu quiz and lecture on MCH.

Table 4 gives the summary of feedback from the students regarding the quiz method. Table 4 shows that higher student satisfaction and retention during competition for subjects. They enjoyed the experience of a new mode of delivery through a quiz. Most of them asked for more quiz competition during different years; the responses were

**Table 2: Winning teams with their performance**

Session and round	Team A	Team B	Team C	Team D
Session I				
Round I	10	10	00	00
Round II	10	10	10	10
Session II				
Round I	20	20	00	10
Round II	20	20	10	00
Session III				
Round I	05	00	05	10
Session IV				
Round I	00	15	00	20
Total	55	75	25	50

**Table 3: Pre-test and post-test evaluation of traditional lecture and quiz on swine flu**

Score range	Number scored in pre-test lecture (%)	Number scored in pre-test quiz (%)	Number scored in post-test lecture (%)	Number scored in post-test quiz (%)
0-20	5 (6.10)	26 (20.98)	4 (4.87)	09 (9.00)
21-40	50 (60.90)	21 (25.92)	36 (43.90)	2 (2.46)
41-60	27 (33.00)	29 (35.80)	40 (48.78)	6 (7.40)
61-80	0 (0.00)	14 (17.28)	2 (2.43)	32 (39.50)
>80	0 (0.00)	0	0 (0.00)	41 (46.55)
Total	82 (100.00)	90 (100.00)	82 (100.00)	90 (100.00)

$\chi^2=5.7$ ,  $df=2$ ,  $P<0.05$ ;  $\chi^2=79.07$ ,  $df=3$ ,  $P<0.001$

**Table 4: Details of feedback given by students**

Feedback	Response
What factors facilitated learning?	Interesting, interactive, informative, innovative different from routine classes, helped them to come prepared, scope for active participation, building healthy competition, strong mode of teaching, more effective, playful education friendly
What factors hindered the learning?	Visual round required reference from outside (internet)
Which round was liked the most?	Rapid fire round, visual round, MCQs and short answer round in decreasing order
Suggestions for improvement?	Quiz method to be used to teach other topics in community medicine. They also suggested having more rounds in each session, especially in visual round

MCQ: Multiple choice question

encouraging. That method facilitate because it ensured active participation of the students, was Interesting, interactive, informative, strong mode of teaching, more effective, helped to build healthy competition among groups, friendly and playful method of education. The factors which hindered learning was that visual round required the reference from outside the source. Suggestions were given about improvement to organize more quiz session for other topics. To include more round in each and every session. Almost 48% of students liked the rapid fire round. 41 (29%) students liked the visual round while 27 (19%) of them preferred the MCQ round, only six students liked the short answer round.

Figure 2 shows that majority of students were satisfied with the new teaching tool and accepted it with ease as it was simple and fun and encouraged them to participate willingly, and there was improvement in their knowledge and practice.

Figure 3 shows that most of the faculty observed that there was active participation, quiz method was easy to understand and can be successfully used as an alternative to the traditional method.

## DISCUSSION

The development of innovative methods is important to improve student performance. The aim of this preliminary study was to ascertain the effectiveness of quiz as an interactive teaching technique in lectures and implement various quizzing activities and evaluate their impact on learning. This study highlights about teaching theories which proved useful in the development of interest of students in contrast to the traditional lecture method. The demographic data was collected in the two study groups to control for confounding factors. Participants were given 2-week period for the preparation before the lecture and implementing the quizzes.

The study covered all competences regarding the topic, and the quiz was arranged to include all aspect. This study suggested that the there was an exceptional improvement in students' performance in the post-test analysis of swine flu quiz and mini-CEX as compared to the didactic lecture on MCH. Similar findings were observed in the study done by Aljezawi and Albashtawy<sup>9</sup> that considerable achieve mentin post-test than retention test for the students in the quiz group, and they scored significantly better than those in the lecture group.

We had also obtained the summary of feedback from the students and faculties regarding the quiz method. They

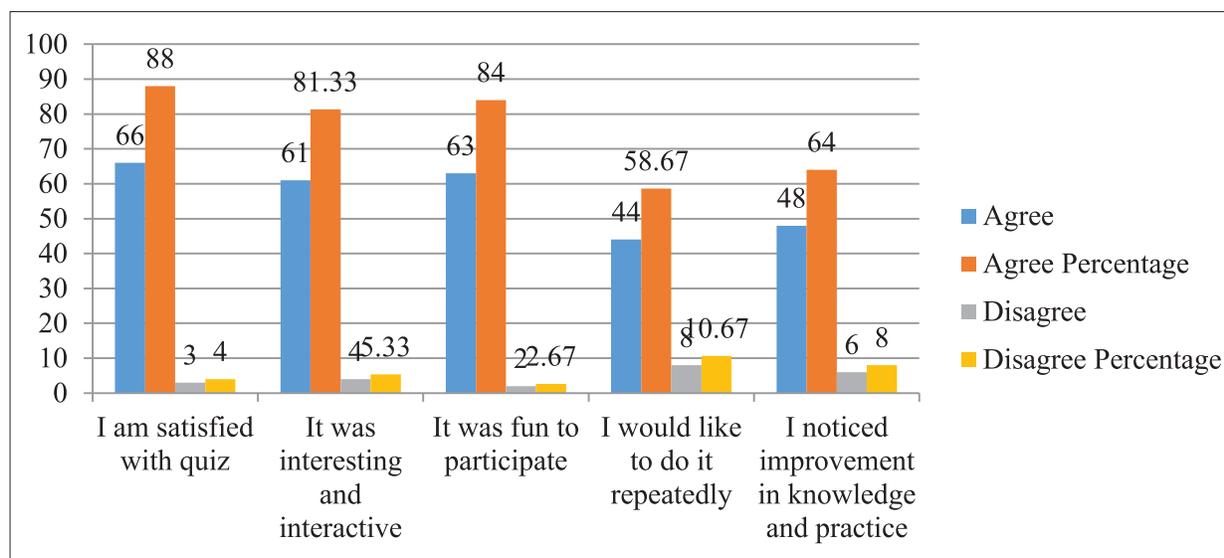


Figure 2: Students perception as per the Likert's scale

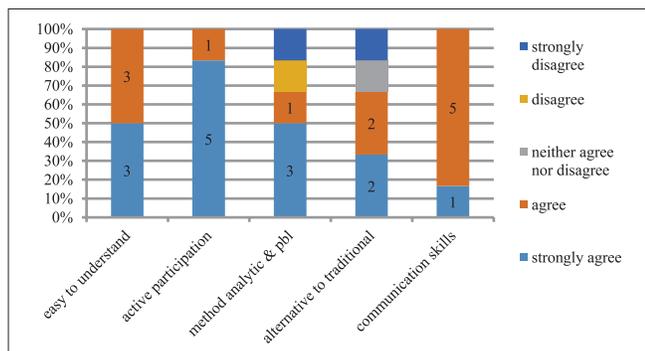


Figure 3: Faculty perception on quiz competition

enjoyed the experience of a new mode of delivery than the traditional method through the quiz. The students response were encouraging, and they asked for the more quiz during different years. The new innovative method of learning had ensured active participation of the students, interesting, interactive, informative, strong mode of teaching, more effective, helped to build healthy competition among groups, friendly and playful method of education. The findings of the study done by Karaksha *et al.*, shown that addition of embedded-animations, as supplement to the traditional didactic lectures, might have a positive impact on student learning, in particular for students who have low grade point average and are challenged by courses that are heavy for the theoretical aspects.<sup>10</sup>

So, it is feasible to adopt interactive teaching in a conventional curriculum in spite of all the challenges like large batches and need to allocate additional teaching hours. However, it needs the proper arrangement of the time frame to complete the due course in time. Moreover, the quiz method allows students to use the internet and other methods for topic preparation in addition to the book.

## CONCLUSION

Quiz is an interactive method of teaching and learning, which gives an opportunity to students for active and student-centered learning. It is feasible to adopt interactive teaching in a conventional curriculum in spite of all the challenges like large batches and need to allocate additional teaching hours. The students find the quiz method to be an interesting and useful learning tool. Students referred optional sources like the internet for preparation. Visual rounds and rapid fire round favored analytical thinking. Quiz nurtures team and competitive spirit. Implementing such interactive techniques requires leadership and team building skills and overcoming logistic barriers.

## LIMITATIONS

Equality of opportunity is less as all the students cannot act as participants in quiz another drawback was that the competition was very much time consuming. Much of the time was spend mainly for framing the questions in the quiz. Hence, this method cannot be organized too frequently.

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# Comparative Analysis of Incidence and Severity of Coronary Artery Disease in Females of Different Age Groups

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## Abstract

**Background:** Coronary artery disease (CAD) is a group of cardiovascular disorders which include stable and unstable angina, myocardial infarctions and sometimes present as sudden cardiac death. It is believed that the males are at more risk of CAD than females but recently it has been found that CAD is becoming the principal cause of death in postmenopausal women universally.

**Materials and Methods:** A total of 240 patients between 25 and 65 years of age were selected for the study at our tertiary care teaching hospital. All vessels were analyzed by quantitative coronary angiography (QCA) using a preinstalled software in the system. The disease severity was analyzed on grounds of the percentage of stenosis of coronary arteries. A coronary artery having stenosis of more than 70% of its diameter or coronary arteries with more than 50% of stenosis on left sided arteries were called as significant stenosis. Based on these parameters we evaluated the stenosis of coronary arteries as single/double/triple vessel disease by QCA.

**Results:** All females underwent angiography out of which 63% were of postmenopausal age, whereas 37% of pre-menopausal age. The most common clinical presentation in both the groups was stable angina. The severity of disease was mild in a premenopausal group, whereas it was more severe in postmenopausal group.

**Conclusion:** The severity and incidence of CAD are more in postmenopausal women as compared to perimenopausal.

**Key words:** Angiography, Coronary artery disease, Peri-menopausal females, Pre-menopausal, Stenosis

## INTRODUCTION

Coronary artery disease (CAD) is a group of cardiovascular disorders which include stable and unstable angina, myocardial infarctions (MI) and sometimes present as sudden cardiac death. The patient usually presents as discomfort or pain in the shoulder, arm, neck and back, heart burn, shortness of breath. Mostly, the symptoms aggravate with exercises and emotional stress, but rest is the relieving factor. The subjects with high blood pressure,

diabetes, obesity, poor nutrition, addiction of nicotine and alcohol are at risk of CAD.<sup>1,2</sup>

In 2013, 8.14 million deaths occurred due to CAD globally, whereas in 1990 the reported deaths due to this disease were 5.74 million. So, CAD is becoming a burden to the society. Studies institute that in developed countries like the United States the risk of death from CAD has decreased between 1990 and 2000. So, it becomes clear that developing countries like India are major contributors of death incidence due to CAD.<sup>3,4</sup>

According to literatures,<sup>3-5</sup> the males are at more risk of CAD than females but recently it has been found that CAD is becoming the principal cause of death in postmenopausal women universally. Many studies favor that, although the rate of occurrence of CAD in premenopausal females is less, but the prognosis is very poor. Mortality rate due to MI for females is

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higher than males for all age groups and poorer for young females.<sup>6,7</sup>

In Framingham Heart Study, 44% of mortality rate was seen in females 1 year after MI as compared to 27% in males.<sup>6</sup> A study done by Women's Ischemia Syndrome Evaluation reports that endogenous estrogen deficiency increases the risk of CAD seven times.<sup>5</sup> Regarding the age, National Health And Nutrition Surveys have found that the incidence of MI is more in 35-54 years in women, while it is less in likewise aged men.<sup>7</sup>

In a recent study conducted in India, it was found that the lifetime possibility of death from CAD is 10 times greater in females than from breast cancer, whereas it is commonly believed that the breast cancer is one of the major causes of mortality in females in developing countries.<sup>8,9</sup>

Various possibilities have been suggested behind the increasing incidence of CAD in women. Studies suggest that smaller vessel size, imprecise electro-cardiographic changes at rest and decrease exercise aptitude might contribute in this respect. Newer risk factors for CAD includes increase levels of lipoprotein A, triglycerides, Apo-B, high level of low density lipoprotein, low levels of high density lipoprotein, increased plasma homocysteine, and C-reactive protein.<sup>9,10</sup>

Micro-vascular abnormalities and diffuse non-obstructive coronary atherosclerosis are more customary in women as compared to men. Angiography is considered as the most essential diagnostic tool, but since non-obstructive CAD is common in women, so the diagnosis of the disease becomes difficult. In premenopausal women acute coronary syndrome which show normal coronary arteries angiographically is also common than men.<sup>9-11</sup>

The aim of present study is to do the comparative study of the severity, clinical presentation of CAD and involvement of coronary arteries in premenopausal and postmenopausal women.

## MATERIALS AND METHODS

After obtaining approval from the Institutional Ethical Committee and due consent from 240 patients between 25 and 65 years of age were enrolled at our tertiary care teaching hospital. The study was conducted between January and December 2014. The patients who refused to give consent for the study, with chronic liver/renal diseases were excluded from the study.

The patients were enquired with symptoms of difficulty in breathing on exertion, chest pain, and any other

cardiac complaints. After thorough history taking and cardiovascular examination, all patients underwent electrocardiogram and echocardiogram on rest. Other routine investigations such as complete hemogram, blood glucose, (random) and renal function tests (blood urea and serum creatinine) were also performed. All cases underwent coronary angiogram (conventional and modified views) and left anterior descending, right coronary and left circumflex arteries were evaluated.

All vessels (individual vessels and their major branches) were analyzed by quantitative coronary angiography (QCA) using a preinstalled software in the system. The disease severity was analyzed on grounds of the percentage of stenosis of coronary arteries. A coronary artery having stenosis of more than 70% of its diameter or coronary arteries with more than 50% of stenosis on left sided arteries were called as significant stenosis. Based on these parameters we evaluated the stenosis of coronary arteries as single/double/triple vessel disease by QCA.

## Statistical Analysis

All data were presented as mean  $\pm$  standard deviation. Student's *t*-test was applied on parametric data. Data analysis was done using SPSS (19 version) software. A *P* < 0.05 was taken as significant.

## RESULTS

During the period of study 240 females underwent angiography out of which 63% were of postmenopausal age, whereas 37% of pre-menopausal age (Table 1 and Figure 1). The most common clinical presentation in both the groups was stable angina. Anterior MI was more common in both the groups as compared to inferior and lateral MI (Table 2 and Figure 2). The mean age of 60.85 years is most common presentation in the postmenopausal females and 37.75 years in the premenopausal. The most common indication for coronary angiogram in both pre and postmenopausal females was unstable angina. However, the second most common presentation in premenopausal females was unstable angina and in postmenopausal females was anterior MI. The least common MI in both the groups is lateral MI. In

**Table 1: Baseline characteristics (mean $\pm$ SD)**

Variables	Premenopausal women (n=90)	Postmenopausal women (n=150)	P value
Mean age (years)	37.75 $\pm$ 6.83	60.85 $\pm$ 7.71	-
Mean systolic blood pressure (mm of Hg)	127.86 $\pm$ 17.31	131.63 $\pm$ 20.17	0.82
Mean diastolic blood pressure (mm of Hg)	78.91 $\pm$ 10.49	82.35 $\pm$ 12.83	0.39

SD: Standard deviation

**Table 2: Clinical presentation of pre/postmenopausal patients presented for CAD**

Clinical presentation	Premenopausal women (n=90)	Postmenopausal women (n=150)
Stable angina	21	56
Unstable angina	19	27
Anterior MI	16	33
Inferior MI	9	10
Lateral MI	3	8
Miscellaneous	22	16

CAD: Coronary artery disease, MI: Myocardial infarction

**Table 3: Severity of CAD in pre/postmenopausal patients**

Severity of CAD	Premenopausal women (n=90)	Postmenopausal women (n=150)
Mild disease	32	15
Single artery disease	29	20
Double artery disease	12	48
Triple artery disease	9	58
Others	8	9

CAD: Coronary artery disease

our study, we found that severity of disease was mild in a premenopausal group, whereas it was more severe in the postmenopausal group (Table 3 and Figure 3).

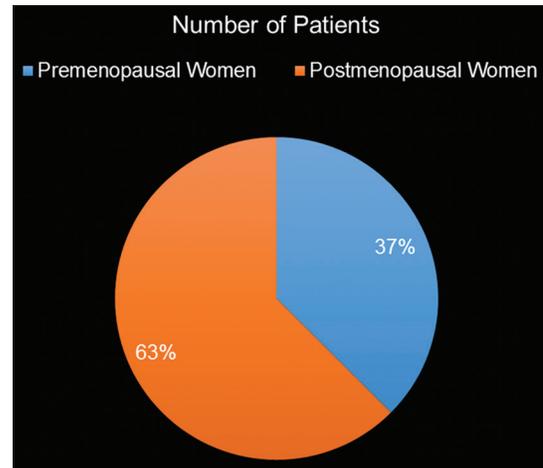
The percentage of triple artery disease is very high (38.6%) in the postmenopausal group but it is very less (10%) in another group. Mild disease is more common in premenopausal group (35.5%) which implies that severity of disease is less in women having regular menstrual cycles.

## DISCUSSION

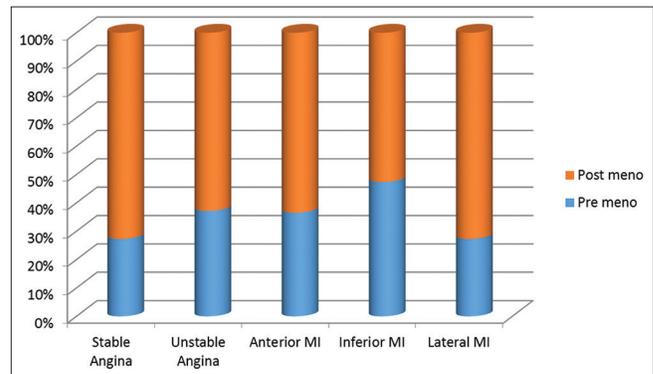
The differences in cardiovascular ailment in males and females advocate a lack of knowledge and awareness among females regarding risk declining efforts. This might be the reason why since 1984, the average figure of deaths from cardiac diseases has been larger for females when compared to males.<sup>12</sup>

Another study recommends that mortality rate after MI is also more in females. Age at the time of clinical presentation and adverse risk factors are two important factors which affect the outcome of disease in females. However, when the risk factors are guarded women also tend to have a better prognosis than men.<sup>13</sup>

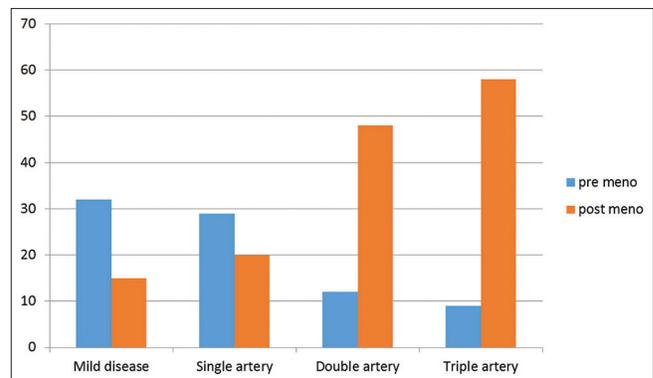
Certain studies suggest that from 1990 to 2020, mortality due to CAD would boost by 38% in men and 30% in women in developed countries. Whereas, in developing countries like India, the mortality rates due to CAD were 127% in females and 130% in males. These percentages



**Figure 1: Number of pre/postmenopausal patients included in the study**



**Figure 2: Comparison (%) of clinical presentations of coronary artery disease in pre and postmenopausal women**



**Figure 3: Comparison of severity of disease in pre and postmenopausal women**

are very high in developing countries as compared to developed one.<sup>9,14</sup>

In our study, most of the female patients of cardiovascular disease who were admitted to hospital with MI were of postmenopausal age. Our findings were supported by another study who reported that the incidence of obstructive CAD is comparatively less before menopause.

Another factor which is considered for higher rate of CAD disease in postmenopausal group is diabetes which is responsible for increasing the severity of disease.<sup>15</sup>

Admission of patients in hospitals with acute coronary conditions was nearly equal in both the groups. However, a study done by Saleh *et al.* on Asian people have shown the high proportion of ST elevation MI among premenopausal women.<sup>16</sup> Various studies suggest that severe CAD including double-vessel and triple vessel diseases were found to be more frequently seen among postmenopausal patients.<sup>15,17</sup>

According to coronary artery surgical study registry, many females with chest discomfort are clinically inseparable from angina pectoris. They had no significant CAD in angiography with 50% presenting non-significant coronary obstruction.<sup>18,19</sup> In our study, most of the women had coronary symptoms, but no definite lesion on angiography was found.<sup>18</sup>

In a later stage, chronic diseases such as hypertension and diabetes show significant augmentation in risk factors in the incidence as well as the severity of CAD. Another study reported that the occurrence of obstructive CAD with stenosis is found in more than 50% of females having cardiac problem. According to age, it includes 27% of women of age <50 years and up to 64% of age 80 years.<sup>7,15</sup>

## CONCLUSION

Though the predictable risk factors play a significant role in the expression of CAD, occurrence of noteworthy CAD in premenopausal women desires further assessment for non-predictable risk factors.

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# Awareness about Non-sexual Modes of Human Immunodeficiency Virus Transmission: A Cross-sectional Study from Tamil Nadu, India

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## Abstract

**Background:** The human immunodeficiency virus/acquired immune deficiency syndrome (HIV/AIDS) epidemic appears to have stabilized in most regions of the globe. Even after all these years of multi-pronged health education campaign, there's still a dearth of awareness about certain aspects of HIV and AIDS. Most of the campaigns have targeted the high risk groups, such as the commercial sex workers, homosexuals, intravenous drug users, and truck drivers. In the majority of these campaigns, greater emphasis was given to educate the people on the sexual mode of transmission.

**Objective:** The objective of present study was to assess the current awareness about the non-sexual mode of transmission of HIV infection.

**Materials and Methods:** Present study was conducted in 4 Primary Health Centre areas in Vellore district of Tamil Nadu. A total of 400 adults from rural areas participated in the study. A pretested questionnaire was used to assess their awareness about HIV transmission.

**Results:** Majority of the study population (86%) knew that HIV is transmitted by sexual intercourse. Whereas, only 50% knew that it can be transmitted from an infected mother to child, and only 36% were aware of the transmission by sharing of syringes and needles. A difference in the awareness level was observed among males and females with regards to HIV transmission by certain non-sexual modes. This was found to be statistically significant ( $P < 0.001$ ).

**Conclusion:** In spite of all the efforts of various international, national, and state agencies, for more than two decades, the awareness level is not excellent. The messages regarding the sexual mode of transmission and condom usage for prevention has reached the masses, but the information about the other modes of transmission and prevention has not reached the common man to the extent of the former.

**Key words:** Human immunodeficiency virus, Non-sexual, Prevention, Transmission

## INTRODUCTION

AIDS, the acronym for acquired immune deficiency syndrome is a fatal disease caused by the retro virus known as human immunodeficiency virus (HIV). Two serological types of HIV has been identified and named as HIV-1 and

HIV-2. HIV-1 is more virulent among these two. Once a person is infected with HIV, he or she is infected for life.

The human transmission of the virus has been documented during the 19<sup>th</sup> or the early 20<sup>th</sup> century. Around 75 million people are infected around the world, and around 36 million have died. The most affected region in the world is the sub Saharan Africa, where 1 in every 20 adults is living with HIV infection.<sup>1</sup> Globally, the heterosexual route is the predominant route of transmission of the virus. Other transmission modes include unprotected penetrative sex between men, sharing of needles among intravenous (IV) drug users, and unsafe blood transfusions for injections.

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In India, HIV infection was first detected in the year 1986.<sup>2</sup> Most of the HIV infections in India occur through heterosexual contact. The rest of the infection occurs among Homosexual (men having sex with men), IV drug users, etc. The epidemic appears to have stabilized in most regions of the globe. However, it continues to increase in some parts of Asia due to high rates of infections. In India, there is a steady decline in the number of AIDS related mortality since 2004, when the free anti-retro viral program was launched in the country.<sup>3</sup>

With the establishment of National Aids Control Organization (NACO) in India, there has been a significant improvement in the country. There has been an overall reduction in the HIV incidence in the country. The prevalence of HIV also varies between different states. Some states in India, including Tamil Nadu, Andhra Pradesh, Telangana, Karnataka, Maharashtra, Nagaland, and Manipur have been reported to have a large number of HIV infected population in India. The AIDS task force in India, under the Indian Council of Medical Research and the National AIDS Committee, fought a multi-pronged campaign to conquer AIDS. As of the year 2009, the prevalence of HIV infection in adults was 0.31%.<sup>3</sup>

Even after all these years of multi-pronged health education campaign, there's still a dearth of awareness about certain aspects of HIV and AIDS. Especially in the rural areas, among the common man, holistic knowledge about HIV has not been disseminated, as most of the campaign has targeted the high risk groups, such as the commercial sex workers, homosexuals, IV drug users, and truck drivers. To quote an example, the India AIDS Initiative, an HIV prevention program which was funded by the gates foundation was implemented in the six states in India where the prevalence was high. This program focused on female sex workers, IV drug users, men who have sex with men, etc. Most of the emphasis was given on the sexual mode of transmission. Hence, the present study was conducted with the aim of assessing the knowledge of a rural adult population on various non-sexual modes of transmission of HIV and its prevention.

## MATERIALS AND METHODS

The present study was done as a cross-sectional study in Vellore district in Tamil Nadu. The district has a land area of around 6000 km<sup>2</sup>, bordering the state of Andhra Pradesh on one side. As per the 2011 census, the population was 3928106. The revenue district of Vellore is further sub divided into two health unit divisions for administrative purposes. The two Health Unit Divisions are Vellore and Tirupattur. The Vellore Health Unit division consists of

10 rural blocks consisting of 35 primary health centers. The present study was done in 4 randomly chosen primary health center areas in Vellore Health Unit division.

An informed consent was obtained from each individual who was willing to participate in the study. Those who did not consent to take part in the study were not included. A female interviewer was present when the questionnaire was administered to a female respondent. A total of 400 individuals participated in this study.

The study questionnaire was designed to elicit certain basic information regarding HIV/AIDS, with emphasis on modes of transmission and prevention. The questionnaire was pretested, and necessary modifications were done before administering on the study population. The data was tabulated and analyzed using SPSS version 17.0.

## RESULTS

The total of 400 adults were enrolled in the present study. There were 220 males and 180 females in the study population. The mean age of the study population was 46, with a minimum age of 23 and a maximum age of 65. When the education status of the subjects was taken into consideration, 60 subjects were illiterate, 284 have gone to some formal school, and 56 have completed college education (Figure 1).

The next important question was about their knowledge regarding the various modes of transmission of the disease. The participants were assessed about their awareness regarding the various modes in which HIV can be transmitted from one individual to another. A majority of them (86%) knew that HIV can be transmitted by sexual intercourse. Around 60% of them also knew that the infection can be transmitted as a result of a blood transfusion (Table 1).

When the respondents were questioned about the different modes of prevention of HIV, the majority of them (88%)

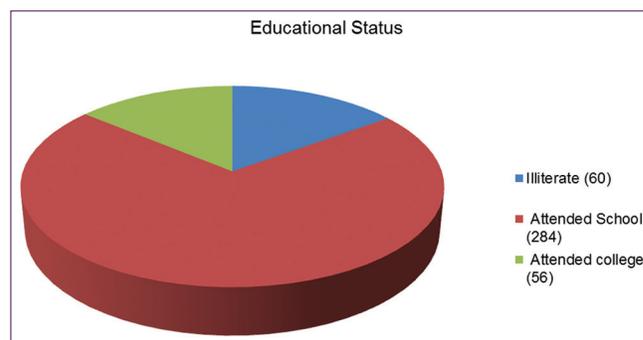


Figure 1: The educational status of the study population

knew that safe sex, i.e. using a condom has a protective effect. The knowledge about the other mode of prevention is given in Table 2.

When the individuals were asked about the source from which they obtained information regarding HIV transmission, majority respondents opined that they received most of their understanding about HIV/AIDS from the mass media. Other sources of information were friends, teachers, and health workers (Figure 2).

The next important question is, whether there is any sex difference with regard to the knowledge or awareness about the transmission of HIV. The present study found out that there is not much of a difference in the level of awareness regarding the heterosexual mode of transmission among men and women. However, there was a wide difference between males and females in the knowledge about HIV transmission by homosexual route, and by way of sharing needles or syringes. This difference was found to be statistically significant (Table 3).

The present study also highlights the prevalence of some common misconceptions regarding the transmission of HIV. Among the respondents, nearly 43% of them thought that HIV can be spread by sharing or eating from the same plate, and another 26% of the respondents were of the impression that HIV can be spread from one person to another while hugging each other.

## DISCUSSION

The present study was done in a sample of the adult population residing in selected primary health center areas of Vellore district in the state of Tamil Nadu. All the respondents had come from a rural background, and

the majority of them had at least school education. It was observed that though most of them had knowledge regarding the sexual mode of transmission of HIV, the awareness about the various non-sexual mode of transmission of HIV was significantly less, in spite of the fact that billions of rupees have been spent on HIV prevention and care in India in the last few decades.

The NACO through the National Aids Control Program has been making great strides in the control of HIV/AIDS spread in the country in the last few decades. The different phases of the National Aids Control Program, supported with internal and external funding from various

**Table 1: The awareness of the respondents regarding the transmission of HIV**

Mode of transmission of HIV	Awareness among the respondents (%)
As a result of heterosexual intercourse with an infected person	344 (86)
As a result of homosexual intercourse with an infected person	180 (45)
During blood transfusion by transfusion of infected blood	248 (62)
Sharing of syringes or needles by IV drug users	144 (36)
Mother to child	200 (50)

IV: Intravenous, HIV: Human immunodeficiency virus

**Table 2: The awareness among the respondents regarding the various modes of prevention of HIV**

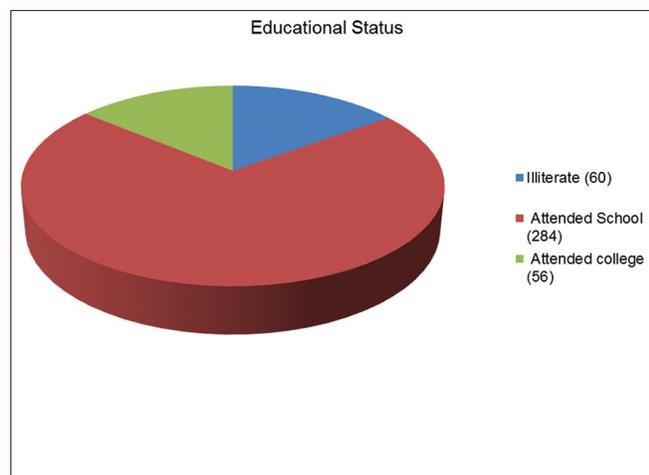
Prevention strategy	Awareness among the respondents
Being faithful to your partner	280 (70)
Using a condom	352 (88)
Safe blood	240 (60)
Not sharing needles or using disposable needles	206 (51.5)

HIV: Human immunodeficiency virus

**Table 3: The sex difference in the level of awareness regarding the modes of transmission of HIV**

Mode of transmission of HIV	Awareness among male respondents (n=220) (%)	Awareness among female respondents (n=180) (%)	$\chi^2/P$ value (df=1)
Heterosexual intercourse with an infected person	190 (86.4)	154 (85.6)	0.054/<0.900
Homosexual intercourse with an infected person	120 (54.5)	60 (33)	17.998/<0.001*
Transfusion of infected blood	148 (67.3)	100 (55.5)	5.769/<0.025*
Sharing of syringes or needles by IV drug users	99 (45)	45 (25)	17.188/<0.001*
Mother to child	105 (47.7)	95 (52.7)	1.010/<0.500

IV: Intravenous, HIV: Human immunodeficiency virus, \*Statistically significant



**Figure 2: The source from which the respondents received information about human immunodeficiency virus transmission**

government and non-governmental agencies, from across the globe, had various Health education campaigns to educate the common man about HIV/AIDS.

Some of the important IEC campaigns were targeted to motivate behavior change among the countrymen. One such example is the red ribbon express, which was an eight coach exhibition on a train, which traveled the length and breadth of the country. They had plenty of halt stations, where the public were allowed to visit the exhibits in the train. From the halt stations, exhibition vans and folk troupes were deployed to carry HIV/AIDS related messages to the rural areas. Apart from this, various multi media campaigns had been conducted. Blood safety campaigns, the establishment of red ribbon clubs in schools and colleges and condom promotion programs were also done. Condoms were available free of cost in most health establishments, and condom vending machines were installed in most public places.

In spite of all these activities at the national and state level, there is a lot to be desired as far as the awareness about HIV/AIDS is concerned, as identified in this study. Other studies also reflect a similar finding. In a study done by Meena *et al.*, the majority of the respondents were aware of the sexual mode of transmission of HIV and that condom usage can prevent the transmission.<sup>4</sup> In a study done by Kotech and Patel, in the slums of Vadodhra in Gujarat, more number of respondents had knowledge of the sexual mode of transmission of HIV than of the other modes of transmission.<sup>5</sup> In another study done by Singh *et al.*, in northern India 79.1% of respondents opined that heterosexual intercourse was the most common mode of transmission.<sup>6</sup>

A study done in a remote location in Jammu and Kashmir shows that the knowledge about HIV transmission and

prevention was very poor.<sup>7</sup> In yet another international study done in Laos, the awareness about the various modes of transmission of HIV/AIDS was significantly high.<sup>8</sup> That study was predominantly conducted among students.

## CONCLUSION

As already discussed, in spite of all these efforts by various international, national and state agencies, for more than two decades, the awareness level is not excellent. The messages regarding the sexual mode of transmission and condom usage for prevention has reached the masses, but the information about the other modes of transmission and prevention has not reached the common man to the extent of the former.

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# Clinical Profile of Bronchial Asthma and its Association to Accessory Nipple

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## Abstract

**Introduction:** Asthma is a very common disease and the presence of extra nipple and breasts known as supernumerary or accessory breast tissue usually found within the milk line is also not uncommon. Various authors found an association of accessory nipple with various systemic anomalies. The present study has been undertaken to clarify some of these conflicting observation in bronchial asthma patients.

**Aims and Objectives:** The purpose of this study was to determine the clinical profile of bronchial asthma and prevalence, familial association, sex and side predilection of the accessory nipple in an asthmatic patient.

**Materials and Methods:** The present study was carried out in the Department of Medicine, Medical College and Associated Hospital, Rewa, Madhya Pradesh, India, from January 2005 to August 2006. Cases selected were all above the age of 15 years and were suffering from bronchial asthma. These patients were subjected to a thorough clinical interrogation, detail physical examination, and laboratory tests. The patients with evidence of organic heart disease, HIV, and respiratory diseases other than bronchial asthma were excluded from this study.

**Results:** In the present study from the sample size of 100 patients of bronchial asthma, the accessory nipple was present in 20% of cases. Prevalence of accessory nipple was more common in males ( $n = 18$ , 23.07%) than in female with bronchial asthma ( $n = 02$ , 9.09%). The family history of bronchial asthma was present in 30% of bronchial asthma patients with accessory nipple as compared to 23.75% of bronchial asthma patients without accessory nipple. Out of 20 patients of bronchial asthma with accessory nipple, 65% ( $n = 13$ ) of patients had accessory nipple on left side along the milk line and 35% ( $n = 07$ ) of patients on right side.

**Conclusion:** There has been an interesting correlation of accessory nipple in bronchial asthma which required further studies to support this observation.

**Key words:** Accessory, Anomalies, Association, Bronchial asthma, Nipple, Supernumerary

## INTRODUCTION

Now a day bronchial asthma is commonly prevalent due to increasing smoking habits, modern life style, and increase air pollution. Though there are various factors causing chronic obstructive lung diseases including genetic factors but the association of bronchial asthma with supernumerary or accessory nipple is of outstanding importance. The presence of extra nipple and breasts,

polythelia and polymastia, respectively, is not uncommon. Such supernumerary breast tissue usually found within the milk line extending from the axilla to the pubic region. Polythelia (congenital supernumerary nipple) is a marker for more serious anomalies of the urinary and cardiovascular system<sup>1</sup> but in many cases, it is probably a chance finding.

Numerous authors have been observed and claim for a close association of supernumerary and a renal anomaly.<sup>2-5</sup> However, a high index of suspicion should be maintained during physical examination because any disease that involved anatomically normal breasts may affect aberrantly located breast or nipples as well. These anomalies may be associated with several systemic disorders. The present study of “clinical profile of bronchial asthma and its association to accessory nipple” has been undertaken to

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clarify some of these conflicting observations and find out evidence to support such an association. The purpose of this study was to determine the clinical profile of bronchial asthma and prevalence, familial association, sex and side predilection of the supernumerary nipple in the asthmatic patient.

## MATERIALS AND METHODS

### Place of Study

This is a cross-sectional prospective clinical observation study. In the present study, 100 bronchial asthma patients were included. The present study was carried out in the Department of Medicine, Shyam Shah Medical College and associated Sanjay Gandhi Memorial (SGM) Hospital, Rewa, Madhya Pradesh, India, from January 2005 to August 2006 within a period of about 20 months. The patients were selected from medical wards, medical out patients department, tuberculosis, and chest clinic of SGM Hospital, Rewa, Madhya Pradesh.

### Inclusion Criteria

Cases selected were all above the age of 15 years and were suffering from bronchial asthma. The criteria for selection of patients were as follows: History of paroxysmal attack of breathlessness, cough and wheeze with symptoms free period of remission, reversal of bronchospasm after administration of bronchodilator, history of allied disorders considered to be allergic in nature, family history of bronchial asthma and other allergic disorder.

### Laboratory Tests

These patients were subjected to a thorough clinical interrogation, detail physical examination, and other laboratory investigations including Spirometry, X-ray chest, and electrocardiography (ECG) also.

### Exclusion Criteria

Persons with evidence of organic heart diseases, HIV, respiratory disease other than bronchial asthma were excluded from this study.

### Statistical Analyses

Results compiled and statistically analyzed with Chi-square and  $P < 0.05$  significance test.

## RESULTS

Out of 100 patients, in the present study, 78% of patients were males and 22% patients were female. The maximum number of patients were in the age group of 21-40 years ( $n = 57, 57\%$ ) and least number of cases below 20 years of age ( $n = 8, 8\%$ ). Out of 100 cases, the majority of patients

were from urban areas for both male ( $n = 49, 62.83\%$  vs.  $n = 29, 37.17\%$ ) and female ( $n = 17, 77.88\%$  vs.  $n = 05, 22.72\%$ ). The majority of cases were found to be laborers (30%) followed by students (23%) and housewives (13%). Out of 100 cases, maximum numbers of patients were from the middle socioeconomic status (53%) and least from the higher socioeconomic status (08%), lower socioeconomic status found to be in 39% of cases. In the present study, majority of the patients (61%) had bronchial asthma of 5-20 years duration. Among these patients most had a mild degree of disease (54.09%), only one patient (1.63%) had a severe degree of disease. The patients with bronchial asthma of <5 years duration had mild degree of disease (69.57%) and patients with bronchial asthma of more than 20 years of duration majority had moderate degree of disease (62.5%). The exacerbation of bronchial asthma had strong relation to seasonal variation ( $n = 73, 73\%$ ) while 27% patients ( $n = 27$ ) had no relation to seasonal variation. The majority of patients had exacerbation of bronchial asthma in winter season ( $n = 57, 78.08\%$ ) followed by rainy season ( $n = 13, 17.80\%$ ) and summer ( $n = 03, 4.11$ ). The most common precipitating factors for acute exacerbation of bronchial asthma were allergens (56%) followed by upper respiratory tract infections (32%) and exercise (04%). There was no history of precipitating factors for acute exacerbation of bronchial asthma in 08% of cases. The exertional or episodic dyspnea was universal symptoms of the illness. As far as other symptoms of bronchial asthma are concerned wheezing was present in 45% cases, cough in 28% of cases, tightness in chest in 21% of cases, and fever only in 06% of cases. In the present study, out of 55 patients of mild degree of bronchial asthma, 14 patients (25.45%) had tachycardia, out of 44 patients who had moderate degree of bronchial asthma 19 patients (43.18%) had tachycardia, as far as severe degree of illness concerned there was single patient of severe bronchial asthma who had tachycardia. All the cases had respiratory rate of more than 16/min and in those 55 patients had mild degree of bronchial asthma, 44 patients had moderate degree of bronchial asthma, and only 1 patient had severe degree of bronchial asthma. Out of 100 patients, cyanosis was present only in 5 cases. Pulsus paradoxus was present only in 1 patient who had severe illness. On auscultation, 55 patients who had mild illness, 40% of patients had rhonchi and 21 patients had vesicular breath sound with prolonged expiratory phase; 44 patients who had moderate illness, 35 patients had rhonchi and 16 patients had vesicular breath sound with prolonged expiration. Only 3 patients had silent chest.

Maximum numbers of bronchial asthma patients were found to be addicted to tobacco (50%). 48% of patients had no addiction. Only 2% patients had history of alcohol addiction. In the present study, maximum patients who took regular treatment for bronchial asthma had a mild

degree of disease ( $n = 39, 70.91\%$ ). On the contrary, most of the patients who did not take treatment or were on irregular treatment had moderate to severe degree of disease ( $n = 25, 56.82\%$ ). There are no reports regarding the prevalence of accessory nipple in asthma.

In the present study, the accessory nipple was present in 20% of cases. Prevalence of accessory nipple was more common in males ( $n = 18, 23.07\%$ ) than in females with bronchial asthma ( $n = 02, 09.09\%$ ) (Table 1).

In the present study, the family history of bronchial asthma was present in 30% of bronchial asthma patients with the accessory nipple as compared to 23.75% of bronchial asthma patients without accessory nipple (Table 2).

In present study, it was found that out of 20 patients of bronchial asthma with accessory nipple, 65% ( $n = 13$ ) had accessory nipple on left side along the milk line and 35% ( $n = 07$ ) of patients had accessory nipple along the milk line on right side. In this study, none of the patients had accessory nipple outside the milk line, as shown in Table 3.

In our study, ECG abnormality was present maximally in patients having bronchial asthma of more than 20 years of duration ( $n = 09, 56.25\%$ ) and least in those having the disease of more than 5-20 years of duration ( $n = 20, 32.72\%$ ). The majority of patients had no radiological abnormalities except changes of hyperinflation of lungs ( $n = 100, 25\%$ ). Pulmonary function test (Spirometry) was done by computerized spirometry. It was observed that patients having duration of bronchial asthma of <5 years had better pulmonary function test (forced expiratory volume in 1 s [FEV<sub>1</sub>]/forced vital capacity [FVC%] pred.  $85.86 \pm 14.70$ ) than those who had duration of bronchial

asthma of more than 20 years (FEV<sub>1</sub>/FVC% pred.  $74.31 \pm 14.13$ ).

**DISCUSSION**

Stone and Wheeler<sup>6</sup> studies the anatomy, physiology, and benign pathology of the nipple and have observed that nipple and areola are pigmented areas of modified skin that connect with the underlying gland of the breast via ducts. The fairly common congenital anomalies of the nipple include inversion, clefts, and supernumerary nipples.

Cinpolat *et al.*<sup>7</sup> had observed and define that an accessory breast with a complete ductal system, areola, and nipple is termed a “supernumerary breast.” Supernumerary nipples are fairly common, but complete supernumerary breasts are rare.

Galli-Tsinopoulou and Stergidou<sup>8</sup> have observed that the supernumerary nipples (or polythelia) usually appear along the embryonic milk lines or in other sites including the back, thigh, vulva, neck, etc. The frequency of polythelia ranges from 0.2% to 5%.

Schmidt<sup>9</sup> observed the prevalence of accessory nipple in a prospective clinical study of 502 individuals, irrespective of disease. Among these 28 (5.6%) exhibited the presence of accessory nipple. The male/female ratio was 20:08. The above observation shown in Table 4, that there was a high prevalence of supernumerary nipple in bronchial asthma (20%) as compared to general population as observed by Schmidt (5.6%). The presence of higher prevalence for male gender in both study groups was found.

In the present study, out of 20 cases, 65% patients ( $n = 13$ ) had accessory nipple on left side along the milk line and 35% ( $n = 07$ ) had accessory nipple along the milk line on

**Table 1: Sex wise distribution of patients with accessory nipple**

Sex	Accessory nipple (N (%))	
	Present	Absent
Male (n=78)	18 (23.07)	60 (76.92)
Female (n=22)	02 (9.09)	20 (90.90)
Total (n=100)	20 (20)	80 (80)

Z=5.6 significant

**Table 2: Accessory nipple and family history of bronchial asthma**

Sex	Family history of bronchial asthma (N (%))		
	Total	Present	Absent
Present	20	6 (30)	14 (70)
Absent	80	19 (23.75)	61 (76.25)
Total	100	25	75

Z=6 significant

**Table 3: Side predilection of accessory nipple**

Side of accessory nipple	Number of patients	Total %
Left side along the milk line	13	65
Right side along the milk line	07	35
Total	20	100

**Table 4: Comparison of present study with prevalence of Accessory Nipple in normal individuals**

Study	Total individuals	Accessory nipple		Total %
		Male	Female	
Schmidt study, 1998 (normal individuals)	502	20	08	5.6
Present study (bronchial asthma patients)	100	18	02	20

right side. None of the patients had accessory nipple outside the milk line. Schmidt<sup>9</sup> also observed 28 individuals with the accessory nipple in which left:right side ratio 15:7 in males and 5:4 in females. Both observations are suggestive of a higher prevalence of accessory nipple on the left side.

Røikjer *et al.*<sup>10</sup> observed that two different forms of ectopic breast tissue exist in human beings: Supernumerary and aberrant. Both forms are usually seen alongside the milk lines, which extend from the upper limbs to the inguinal region where they give rise to mammary glands, areolas, and nipples.

In present study, family history of bronchial asthma was present in 30% ( $n = 19$ ) of bronchial asthma patients without accessory nipple.

Osswald *et al.*<sup>11</sup> also observed that supernumerary breasts and nipples are not uncommon and have familial and syndrome associations.

According to Vishwanathan and Shourie<sup>12</sup> incidence of bronchial asthma was higher in patients of asthmatic parents and there is some evidence of hereditary predisposition of this illness.

According to Toumbis-Ioannou and Cohen<sup>13</sup> in their observations familial cases were recorded as parent child transmission, including one report of a family who had supernumerary nipples in four successive generations therefore, autosomal dominant with incomplete expressivity is the accepted transmission of inheritance.

According to Urbani and Betti,<sup>14</sup> multi-generation involvement was the rule. Cellini and Offidani<sup>15</sup> in their case report observed three cases of supernumerary nipple in the same family and found the familial tendency of supernumerary nipple.

Urbani and Betti<sup>5</sup> observed association between supernumerary nipple with kidney and urinary tract malformations. They were observed in 146 white patients (123 men, 23 women) with accessory mammary tissue out of 2645 subject consecutively referred for physical examination. Kidney and urinary tract malformation were detected in 11 patients with accessory mammary tissue (09 men, 02 women) and in one control. These data show a significantly higher frequency of kidney and urinary tract malformation in patients with accessory mammary tissue as compared to controls (7.53% vs. 0.68%  $P < 0.001$ ).

Grimshaw and Cohen<sup>16</sup> observed that the presence of supernumerary nipples, known as polythelia, is the most common presentation of accessory breast tissue. It is

usually considered to be a benign congenital anomaly. However, polythelia may warrant attention for more than mere cosmetic concern because supernumerary nipples have been shown to be associated with an increased risk of genitourinary malignancies.

Pellegrini and Wagner<sup>17</sup> also observed that congenital supernumerary nipple is a marker for more serious anomalies of the urinary and cardiovascular systems. It is associated with obstructive abnormalities of the kidney or the renal collecting system, renal, cardiac conduction disturbances, and congenital heart disease.

Rajaratnam *et al.*<sup>18</sup> observed 68 Asian Indians from South India with supernumerary nipple and 49 age and sex matched controls without supernumerary nipple for evidence of mitral valve prolapsed and associated features. He found that mitral valve prolapsed were more common in the supernumerary group (odd ratio 6.0, 95% confidence intervals 2.16-16.63), indicating an association of supernumerary nipple with mitral valve prolapse.

As this interesting observation of supernumerary nipple in bronchial asthma has not been reported in the literature, hence it required more such studies to substantiate this finding.

## CONCLUSION

There has been an interesting correlation of accessory nipple in bronchial asthma which requires further studies to support this observation. Index of suspicion should be maintained during the physical examination that aberrantly located breast and accessory nipple may be associated with bronchial asthma along with the other systemic disease.

Hence it can be concluded that male sex, advancing age, usual residence in urban area, middle socioeconomic status, history suggestive of atopy, family history of asthma, and all forms of tobacco smoking were associated with significantly higher odds of having asthma. The rapid rise in the prevalence of asthma, particularly over a relative short time frame, suggests that environmental rather than genetic factors are important in the development and/or the persistence of the disease. This has focused a significant body of effort into epidemiological research programs that may identify causative factors. It is hoped that some of these may be potentially modifiable.

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# Periodontal Infection Modifying Radiation Mucositis in Patients Receiving Radiation Therapy

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## Abstract

**Background:** The severity of mucositis varies and depends on factors such as the dose of irradiation, anatomic site of irradiation, and other factors which are attributed as the patient sensitivity to the therapy. Investigators are in constant pursuit of exploring regarding the factors responsible for onset, variability of distribution and severity of mucositis in the oral cavity during irradiation. This variable distribution of mucositic lesions led investigators to evaluate other contributing factors for the initiation and aggravation of radiation-induced mucositis.

**Materials and Methods:** The present clinical study evaluates the correlation of the influence of periodontitis in modifying mucositis during radiation therapy of oropharyngeal carcinoma patients. The aim of the study was to evaluate the definitive influence of periodontal status in modifying the progress of mucositis during radiation therapy and also to compare the efficacy of povidone iodine (5% w/v) and chlorohexidine gluconate 0.2% for controlling radiation-induced mucositis in patients with oropharyngeal cancer.

**Results:** In the 2<sup>nd</sup>, 3<sup>rd</sup>, 4<sup>th</sup>, and 5<sup>th</sup> weeks, the values of Pearson co-efficient of co-relation were 0.62 and 0.73, 0.31, and 0.07, respectively, indicating a positive co-relation between periodontal index and mucositis index.

**Conclusions:** The periodontal disease is one, among the various contributing factors responsible for the initiation and degree of severity of radiation mucositis during treatment of oropharyngeal cancer.

**Key words:** Irradiation, Mucositis, Oropharyngeal carcinoma, Periodontal status, Radiation

## INTRODUCTION

Radiation mucositis is defined as an inflammatory like the process of the oropharyngeal mucosa following therapeutic irradiation of patients who have head and neck cancer. The patients undergoing radiation treatment for malignant neoplasms of the oral cavity suffer a great deal of discomfort in speech, mastication, deglutition, and salivation because of these lesions.<sup>1</sup> Oral complications are painful, diminish the quality of life and may lead to

significant compliance problems, often discouraging the patients from continuing treatment.<sup>2</sup> One contributing factor to the development of fatal infection is also described to be radiation-induced mucositis.<sup>3</sup> Previous studies have observed that it is not possible to account for the onset, variability of distribution and severity of mucositis in the oral cavity during irradiation.<sup>4</sup> This variable distribution of mucositic lesions from the data obtained in the studies of various authors led investigators to evaluate other contributing factors to the initiation and aggravation of radiation-induced mucositis. Oral flora is thought to contribute to irradiation mucositis.<sup>5</sup> Moreover, negligence of oral hygiene may also contribute to mucositis. Even if oral hygiene measures are being instituted in the presence of oral diseases, there are greater chances of increase in the number and imbalance of the oral flora.<sup>5</sup> In previous literatures, a positive correlation between the presence of mucositis and radiation therapy

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is present but there is a lack of correlation between the various factors inducing and aggravating it. Here, in this study, it has been attempted to enquire whether any relationship exists between pre-existing periodontal disease and initiation or aggravation of mucositic lesions during radiation therapy, where the oral cavity is not free from infection and inflammation. Keeping all the above factors in mind, present clinical study was designed with the following aims and objectives:

### Aims and Objectives

1. To establish and correlate the definitive influence of periodontal status in modifying the progress of mucositis in patients receiving radiation therapy of head and neck region
2. To correlate the distribution of initial lesions of mucositis to different causative factors
3. To compare the effects of different antimicrobial agents for the elimination of pathogenic microbial flora to control mucositis during radiation therapy
4. To evaluate the need of periodontal treatment in the pre-treatment program before radiation therapy.

## MATERIALS AND METHODS

The sample for the present study comprised of 80 patients of oropharyngeal carcinoma selected for irradiation, attending AHRCC, Cuttack. The patients were selected irrespective of age, sex, and stage of the disease. The sample size was selected after consulting the statistician.

Inclusion criteria of these patients were as follows:

- i. Oropharyngeal carcinoma patient selected for radiation therapy
- ii. All patients were treated by Co-60
- iii. All patients received the same provisional total dose of radiation; i.e., 60Gy
- iv. All patients were treated by same fractionation daily dose of 200 cGy, for 5 days a week
- v. All patients were having a provisional overall time of 6 weeks radiation protocol treatment
- vi. None of the patients was completely edentulous
- vii. Irradiation portals include teeth, oral mucosa, and salivary glands.

The treatment outlined by the oncology team was based on the type of radiation treatment to be instituted, differing from each other according to different stages of the disease.

The neoplasm included, were from all the stages.

Stage I:  $T_1 N_0 M_0$ ,  
Stage II:  $T_2 N_0 M_0$ ,

Stage III:  $T_3 N_0 M_0$ ,  $T_{1-2,3} N_1 / M_0$ ,  
Stage IV:  $T_4 N_0 M_0$ ,  $T_{any} N_{any} M_{any}$

All patients received a thorough dental examination before instituting radiotherapy. All patients were given oral prophylaxis. Extraction of mobile cariously exposed and grossly decayed teeth were done 1 week prior to instituting radiotherapy.

During radiation, only fluoride gel therapy was instituted for all.

Artificial saliva (carboxy methyl cellulose preparations) was given to those patients who complained about the dryness of the mouth.

The patients were then divided into two groups:

1. Study group: Included those patients, who were suffering from periodontitis
2. Control group: Included those patients, who were not suffering from any kind of periodontal diseases.

### Study Group

Only the hopeless, mobile, grossly decayed, and cariously exposed teeth were extracted. All patients were given oral prophylaxis.

No attention was given to observe the resolution of periodontal inflammation before irradiation. Smoothing of sharp cusps was also done in some patients, whenever required. During radiation therapy, partially edentulous patients were advised not to wear their removable prosthesis.

This group was again sub-divided into two subgroups:

- $S_1$ : Using chlorohexidine gluconate 0.2%.
- $S_2$ : using povidone iodine 5% w/v mouth rinse.

Each subgroup consisted of 20 patients.

### Control Group

Oral prophylaxis and root planning were done for these patients.

It was strictly observed that periodontally involved teeth were present in the oral cavity and that periodontal inflammation was completely resolved before initiation of radiation therapy.

Furthermore, it was strictly observed that no carious exposed or periapically diseased teeth existed in the oral cavity.

Orthopantomograph was taken for all these patients. It was observed that all teeth present were apparently free

from inflammation and depth of their gingival sulci was not more than 2 mm.

### Other Measures

1. Patients using removable partial denture were not allowed to wear the denture.
2. Smoothing of sharp restoration and cusps was done.

Variables used are: The scores of mucositis index, Russell's periodontal Index, which were recorded at weekly interval.<sup>6,7</sup>

## RESULTS

### Mucositis Index

Table 1 shows the profile baseline characteristics of the patients. The average mucositis index scores for both control and study groups are illustrated in Table 2. This Table 2 shows the average mucositis of all the groups at each week interval. Table 3 elucidates the average mucositis index values of study Subgroup 1 and control group along with their standard deviations for comparison of mucositis index in both the groups. The difference show, however, was statistically significant at 5% level of significance  $P < 0.05$ , indicating that the degree of mucositis was greater in the study Subgroup 1, despite the use of chlorohexidine gluconate mouth rinse. Table 4 shows average mucositis index of study Subgroup 2 and control group along with their standard deviation and the difference between these two groups. Variables were assessed by Student's *t*-test. Here also the difference was significant.

Table 5 compared mucositis index between study Subgroups 1 and 2, and it was found to be not significant.

### Correlation between Mucositis Index and Periodontal Index

Table 6 showed the average value of periodontal index and mucositis index of study Subgroup 1. Table 7 showed the average values at each week interval, the standard deviation along with the Pearson co-efficient of co-relation. During the 1<sup>st</sup> week, mucositis index was found to be 0. Thus it could

not be correlated with the periodontal index. In the 2<sup>nd</sup> and 3<sup>rd</sup> weeks, the values of Pearson co-efficient of co-relation were 0.62 and 0.73, respectively, indicating a positive co-relation between periodontal index and mucositis index. During the 4<sup>th</sup> and 5<sup>th</sup> week, the values of co-efficient of co-relation were 0.31 and 0.07, respectively, which also indicates a positive correlation between periodontal index and mucositis index. However, the correlation is of better degree during the 2<sup>nd</sup> and 3<sup>rd</sup> week than during the 4<sup>th</sup> and 5<sup>th</sup> weeks. Table 8 showed average value of periodontal index and mucositis index of study subgroup-2. Table 9 showed the co-relation between the periodontal index and mucositis index for the study Subgroup 2. In the 2<sup>nd</sup> and 3<sup>rd</sup> week, the co-efficient of co-relation were found to be 0.6 and 0.38, respectively, indicating a positive co-relation between periodontal index and mucositis index. During the 4<sup>th</sup> and 5<sup>th</sup> week, these values were found to be 0.327 and 0.09, respectively, which also indicates a positive co-relation between the two indices.

## DISCUSSIONS

The concept that "Radiation Mucositis" is the direct effect of radiation.<sup>8</sup> The statement was reinforced later by Rosenthal and Wilkie,<sup>9</sup> Baker<sup>10</sup> and Tikriti *et al.*

The variability of occurrence and distribution led others to think about the contributing factors. It is found that vascular changes occurring during radiation therapy decrease the blood supply of the tissue, which reduces the ability of the tissue to withstand trauma and infection.<sup>11</sup> It is again confirmed the fact that minimal trauma within the field of irradiation could cause ulcerations which might take a month to heal and often lead to exposure of bone.<sup>12</sup> New evidence supports the view that oral mucositis is a complex process involving all the tissues and cellular elements of the mucosa. Other findings suggest that some aspects of mucositis risk may be determined genetically. GI pro-apoptotic and anti-apoptotic gene levels change along the GI tract, perhaps explaining differences in the frequency with which mucositis occurs at different sites. Spijkervet *et al.*<sup>13</sup> concluded that oral hygiene may also contribute to mucositis. In 1991, he reported about the role of gram negative bacilli or endotoxin in the pathogenesis of mucositis during irradiation. Although direct cell damage from radiation therapy initiates the process, evidence suggests that the pathogenesis of mucositis is more a complex phenomenon.<sup>14</sup> The five stage model that has been proposed, includes (1) reactive oxygen species, (2) second messengers, (3) proinflammatory cytokines, (4) pathways evading host defense, and (5) metabolic by products of colonizing microorganisms. This model is believed to play a role in amplifying tissue injury.<sup>15</sup>

**Table 1: Profile of baseline characteristics**

Characteristics	Numbers
Number of patient enrolled	40
Number of patients treated	40; 20 (S)+20 (C)
Number of patients followed up	40
Sex ( <i>n</i> =40)	
Female	5
Male	35
Age	
Range (years)	
18-30	2
35-70	38

S: Study, C: Control

**Table 2: Average Spijkervet’s MI patient wise at different phases**

Study group						Control group					
Patient number	Week					Patient number	Week				
	I	II	III	IV	V		I	II	III	IV	V
Subgroup 1						Control					
1	0	2.01	2.05	4.06	4.88	1	0	0.501	0.602	0.701	0.86
2	0	1.53	1.57	2.7	2.88	2	0	0.620	0.701	0.803	0.9
3	0	1.63	2.7	3.95	4.13	3	0	0	0	0	0
4	0	1.63	1.67	3.95	4.13	4	0	0.701	0.803	0.901	1.05
5	0	1.41	1.45	2.7	2.88	5	0	0.401	0.504	0.603	0.75
6	0	1.43	1.47	3.45	3.63	6	0	0	0	0	0
7	0	1.01	1.65	3.2	2.88	7	0	1.18	1.202	1.301	1.40
8	0	1.71	1.75	3.7	3.88	8	0	0	0	0	0
9	0	1.14	1.15	3.7	3.88	9	0	0.01	1.01	1.101	1.25
10	0	1.01	1.05	4.1	4.38	10	0	0.751	0.85	0.9501	1.10
Subgroup 2											
1	0	2.101	2.201	4.701	4.75	11	0	1.201	1.301	1.301	1.60
2	0	1.621	1.721	2.601	2.75	12	0	0	0	0	0
3	0	1.721	1.821	3.851	4.02	13	0	1.011	1.101	1.101	1.35
4	0	1.721	1.821	3.851	4.01	14	0	1.001	1.101	1.101	1.35
5	0	1.501	1.601	2.601	2.75	15	0	0	0	0	0
6	0	1.623	1.623	3.351	3.59	16	0	0.251	0.351	0.452	0.601
7	0	1.101	1.201	3.101	3.25	17	0	0.351	0.451	0.551	0.701
8	0	1.801	1.901	3.601	3.75	18	0	0	0	0	0
9	0	1.201	1.301	3.601	3.75	19	0	0.401	0.501	0.601	0.751
10	0	1.101	1.201	4.101	4.25	20	0	0.501	0.601	0.701	0.851

MI: Mucositis index

**Table 3: Comparison of MI between study subgroup 1 and control group**

Week	Study subgroup 1	Control group
<b>II</b>		
Average	1.484	0.44
SD	0.309	0.402
t-value	26.84	
Statistical significance		S
<b>III</b>		
Average	1.48	0.55
SD	0.307	0.403
t-value	9.84	
Statistical significance		S
<b>IV</b>		
Average	3.7	0.62
SD	0.317	0.408
t-value	32.42	
Statistical significance		S
<b>V</b>		
Average	3.8	0.77
SD	0.311	0.41
t-value	31.56	
Statistical significance		S

SD: Standard deviation, S: Significance, MI: Mucositis index

**Table 4: Comparison of MI between study subgroup 2 and control group**

Week	Study subgroup 2	Control group
<b>I</b>		
Average		
SD	0	0
t-value		
Statistical significance		
<b>II</b>		
Average	1.53	0.44
SD	0.298	0.402
t-value	7.17	
Statistical significance		S
<b>III</b>		
Average	1.63	0.55
SD	0.308	0.403
t-value	7.6	
Statistical significance		S
<b>IV</b>		
Average	3.52	0.62
SD	0.311	0.402
t-value	12.07	
Statistical significance		S
<b>V</b>		
Average	3.67	0.77
SD	0.307	0.41
t-value	19.59	
Statistical significance		S

SD: Standard deviation, S: Significance, MI: Mucositis index

A variety of interventions has been assessed for preventing oral mucositis or reducing the severity of mucositis and its sequelae. These include meticulous pre radiation on going mouth care, calcium phosphate solution, near-infrared light and lower-energy laser treatment, interleukin-11, sucralfate, oral glutamine, granulocyte-macrophage colony-stimulating factor rinse, tretinoin, and keratinocyte growth factor.<sup>16</sup> Particularly, promising results have been observed

with the use of the cytoprotectant/radioprotectant agent amifostine.<sup>16</sup> To the best of our knowledge, palifermin (keratinocyte growth factor-1) is the only agent that has been approved as a drug by the United States Food and

**Table 5: Comparison of MI between study subgroup 1 and study subgroup 2**

Week	Subgroup 1	Subgroup 2
I		
Average	0	0
SD		
t-value		
Statistical significance		
II		
Average	1.44	1.53
SD	0.3089	0.298
t-value	0.608	
Statistical significance		NS
III		
Average	1.48	1.63
SD	0.307	0.308
t-value	0.258	
Statistical significance		NS
IV		
Average	3.7	3.52
SD	0.317	0.311
t-value	0.72	
Statistical significance		NS
V		
Average	3.8	0.77
SD	0.311	0.41
t-value	0.706	
Statistical significance		NS

SD: Standard deviation, S: Significance, NS: Not significance, MI: Mucositis index

**Table 6: Average values of PI and MI of study subgroup 1**

Patient number	Week									
	I		II		III		IV		V	
	MI	PI	MI	PI	MI	PI	MI	PI	MI	PI
1	0	5.1	2.01	5.1	2.05	5.2	4.6	5.8	4.88	5.88
2	0	4.8	1.53	4.8	1.57	4.9	2.7	5.55	2.88	6.63
3	0	5.3	1.63	5.3	1.67	5.4	3.95	6.05	4.13	6.13
4	0	4.1	1.63	4.1	1.67	4.2	3.95	4.8	4.13	4.88
5	0	8.9	1.41	3.9	1.45	4.0	2.7	4.65	2.88	4.63
6	0	4.1	1.43	4.1	1.47	4.2	3.95	4.8	3.63	4.88
7	0	4.3	1.01	4.3	1.65	4.4	3.2	5.0	2.88	5.13
8	0	3.6	1.71	3.6	1.75	3.7	3.7	4.3	3.88	4.38
9	0	3.3	1.14	3.3	1.15	3.4	3.7	4.05	3.88	4.13
10	0	3.1	1.01	3.1	1.05	3.2	4.1	3.8	4.38	3.88

MI: Mucositis index, PI: Periodontal index

Drug Administration and the European Medicines Agency for oral mucositis.<sup>17</sup> There was adequate positive evidence to support a suggestion in favor of using oral care protocols for the prevention of oral mucositis. The evidence also supported the use of chlorohexidine mouthwash for the prevention of oral mucositis in patients receiving radiotherapy.<sup>18</sup> Other agents used are; antimicrobials, coating agents, anesthetics, anti-inflammatory-analgesics, natural miscellaneous agents like zinc supplements. Laser, light therapy, and cryotherapy are also used for management of mucositis. With this back ground of information, the

**Table 7: Correlation between periodontal index and mucositis index of study subgroup I**

Week	PI	MI
I		
Average	4.1	
SD	7.25	0
II		
Average	4.1	1.44
SD	0.725	0.309
r=0.62		
III		
Average	4.87	1.48
SD	0.74	0.307
r=0.73		
IV		
Average	4.87	3.7
SD	0.76	0.317
r=0.317		
V		
Average	4.95	3.8
SD	0.75	0.311
r=0.07		

MI: Mucositis index, PI: Periodontal index, SD: Standard deviation

**Table 8: Average values of PI and MI of study subgroup 2**

Patient number	Week							
	I		II		III		IV	
	PI	MI	PI	MI	PI	MI	PI	MI
1	5.3	0	5.3	2.1	5.4	2.2	5.6	4.7
2	5.0	0	5.0	1.620	5.15	1.72	5.35	2.6
3	5.5	0	5.5	1.720	5.65	1.82	5.85	3.85
4	4.3	0	4.3	1.720	4.4	1.82	4.6	3.851
5	4.05	0	4.05	1.502	4.15	1.601	4.35	2.601
6	4.3	0	4.3	1.52	4.4	1.62	4.6	3.35
7	4.5	0	4.5	1.101	4.65	1.2	4.85	3.1
8	3.8	0	3.8	1.8	3.9	1.9	4.1	3.6
9	3.5	0	3.5	1.2	3.65	1.3	3.85	3.6
10	3.3	0	3.3	1.1	3.4	1.2	3.6	4.1

MI: Mucositis index, PI: Periodontal index

present investigation was conducted to correlate clinically the initiation and progress of irradiation oral mucositis with pre-existing periodontal infection.

Mucositis index in 1<sup>st</sup> week could not be correlated to periodontal index as no mucositis appeared during the 1<sup>st</sup> week of radiation in this study. Toward the end of the 2<sup>nd</sup> week mucositis index was significantly correlated with periodontal index, as the area of distribution showed that mucositis started developing around the teeth with greater degree of periodontal disease.

In the 3<sup>rd</sup> week, the lesions started spreading to other surrounding areas while some lesions started in the area more susceptible to trauma. In this week, also a significant correlation was found.

**Table 9: Correlation between PI and MI of study subgroup 2**

Week	PI	MI
I		
Average	4.35	
SD	0.698	0
<i>r</i> - could not be correlated		
II		
Average	4.34	1.53
SD	0.709	0.298
<i>r</i> =0.6		
III		
Average	4.47	1.63
SD	0.706	0.308
<i>r</i> =0.38		
IV		
Average	4.67	3.52
SD	0.698	0.311
<i>r</i> =0.327		
V		
Average	4.82	3.67
SD	0.712	0.308
<i>r</i> =0.09		

MI: Mucositis index, PI: Periodontal index, SD: Standard deviation, *r*: Pearson co-efficient of correlation

During the 4<sup>th</sup> week, the lesions were spread to other areas, increasing the severity of mucositis index. However, here, the correlation between periodontal index and mucositis index declined which could have been due to other contributing factors such as poor oral hygiene and trauma. In the 5<sup>th</sup> week also the correlation further declined between mucositis index and periodontal index, which could also have been due to the other contribution factors as described before. However, the co-relation is of better degree during 2<sup>nd</sup> and 3<sup>rd</sup> week than during the 4<sup>th</sup> and 5<sup>th</sup> weeks.

It can thus be suggested that though radiation mucositis occurs during irradiation, its initiation and severity cannot be solely attributed to the dose of radiation. As per the present observation, periodontal infection in the form of periodontitis can be considered as an initiating factor in the development of mucositis. Neither of the antimicrobial agents *viz.*, chlorohexidinegluconate nor povidone-iodine (5% w/v) are effective in controlling the severity of mucositis during radiation therapy in patients suffering from oropharyngeal cancer.

The stages of the pathogenesis of periodontal disease involve the process of Colonization–Invasion–Destruction.

Irradiation reduces the vascularity of tissue thereby compromising the local defense mechanism inherent in the healthy mucosa. This factor along with the decrease turnover of mucosa; could make it easier for the invasion of the adjacent mucosa around periodontally involved teeth by the periodontopathic micro-organism. This

postulation could possibly be considered as a reason for the development of mucositis around the periodontally compromised teeth.

## CONCLUSIONS

The periodontal disease is one of the contributing factors responsible for the initiation and degree of severity of radiation mucositis during treatment of oropharyngeal cancer.

The radiation-induced mucositis lesions were found to develop around periodontally involved teeth especially during the 2<sup>nd</sup> and 3<sup>rd</sup> weeks of the irradiation period indicating a positive correlation between the degree of mucositis and periodontal status during this period. As the oral hygiene maintenance level of the patient falls, and the periodontitis develops, there is an increase in the progress and severity of the mucositis lesions. Neither of the antimicrobial agents *viz.*, chlorohexidine gluconate nor povidone-iodine (5% w/v) are effective in the control of the severity of mucositis during radiation therapy in patients suffering from oropharyngeal cancer. It can thus be stated that there exists a definitive influence of the infection and inflammation associated with periodontitis in modifying the initiation and progress of radiation-induced mucositis in patients suffering from oropharyngeal cancer.

Hence, it may be advised that in consultations with the oncology team, treatment procedure aimed at improvement of the overall periodontal health and oral hygiene status of patients suffering from oropharyngeal cancer should be instituted and completed satisfactorily prior to the radiation protocol period to prevent the initiation and progression of radiation - induced mucositis in these patients.

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# Outcomes of Percutaneous Medial-Lateral Cross Pinning of the Pediatric Supracondylar Fractures of the Humerus

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## Abstract

**Introduction:** Supracondylar fracture of distal humerus is the commonest pediatric fractures around the elbow. Treatment options range from non-operative to the closed or open reduction of the fracture and percutaneous Kirchner-wire (K-wire) fixation depending upon fracture and patient variables and expertise available. There are various patterns of percutaneous K-wire fixations described by different authors. The rate of traumatic and iatrogenic ulnar nerve injuries following pediatric supracondylar fractures of the humerus ranges from 12% to 20% and 2% to 6% respectively. The present study is aimed at determining the various outcomes in patients with pediatric supracondylar fractures of the humerus treated by close reduction and a medial-lateral percutaneous K-wire fixation.

**Materials and Methods:** Thirty five children with Gartland Type II and III supracondylar fracture of humerus were treated between February 2009 and December 2014 by closed reduction and percutaneous medial-lateral cross K-wire fixation. There were 22 male and 13 female children. Mean age of the children was 6.9 years (range 3-15 years) Extra care was taken to identify and secure the ulnar nerve while inserting the medial pin. All the patients were followed for a mean period of 9.4 months (range 6-13 months).

**Results:** Union was seen in all patients (100%) at a mean interval of 4.5 weeks (range 3-5 weeks). One patient (2.9%) had varus union. Superficial pin tract infection was seen in 5 (14.2%) patients. None of the patients has a pre-operative ulnar nerve injury, while 1 (2.9%) patient had iatrogenic ulnar nerve neurapraxia. Based on Flynn's criteria 85.6% patients had good to excellent results, 8.6% patients had fair results while 5.8% had poor results.

**Conclusion:** Pediatric supracondylar fractures can be satisfactorily treated by close reduction and percutaneous medial-lateral cross K-wire fixation without any undue risk of ulnar nerve injury.

**Key words:** Child, Closed reduction, Fracture fixation, Humerus, Ulnar nerve

## INTRODUCTION

Supracondylar fracture of the humerus is the second most common pediatric fracture and account for 16% of all pediatric fractures. Pediatric supracondylar fractures of

the humerus with an incidence rate of 65.4% constitute the most common pediatric elbow fractures.<sup>1</sup> The peak age of the fracture is at 5-7 years of age.<sup>2</sup> During this age there is intense remodeling taking place at the distal end of humerus making it thinner and more prone to fracture in the supracondylar area.<sup>3</sup> The usual mode and mechanism of injury involve a high velocity injury in the form of a road traffic accident or a fall from a height with hyperextension or flexion at elbow and supination or pronation at the radioulnar joint.<sup>4,5</sup> Extension type of supracondylar fracture is most common with an incidence of 95%, followed by less common flexion type of supracondylar fracture. Gartland classified the pediatric supracondylar fractures

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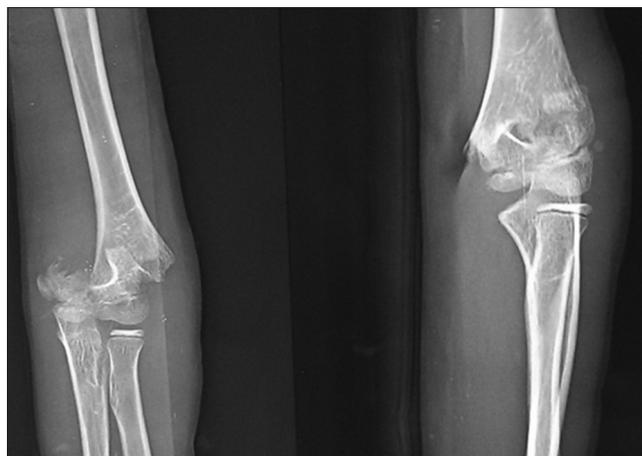
of the humerus into three types based on the degree of displacement, which was letter modified by Wilkins.<sup>4,6</sup> The available treatment options range from conservative to closed and or open reduction and percutaneous Kirchner-wire (K-wire) fixation depending upon the age of the patient, displacement, and duration of fracture and the expertise available.<sup>4</sup> Percutaneous K-wire fixation can be inserted either in a medial-lateral fashion or thorough a lateral entry only with each method having its own merits and demerits.<sup>7,8</sup> Failure to execute a timely and appropriate treatment plan for these fractures may lead to various complication including, varus malunion, elbow stiffness, Volkmann ischemic syndrome/contracture, neurovascular injury, myositis ossificans, etc.<sup>9-12</sup>

## MATERIALS AND METHODS

This was retrospective study that included the pediatric patients with acute supracondylar fracture of humerus operated between February 2009 and December 2014 at a tertiary care institute. There were 22 male and 13 female patients. Mean age of the patients was 6.9 years (range 3-15 years). Inclusion criteria were fresh ( $\leq 7$  days), traumatic, extension type, supracondylar fractures in children  $< 15$  years of age. Exclusion criteria were neglected ( $\geq 7$  days), fractures complicated by open wounds or neurovascular injury, irreducible fracture by the closed method and patients having age of more than 15 years. The study was started after approval by the Institutional Ethical Committee. An informed written consent was obtained from all the study participants. A thorough clinical history and detailed examination with particular emphasis on neurovascular component was done for all the patients, followed by plain radiological examination of the injured elbow including anteroposterior (AP) and lateral views (Figure 1).

### Surgical Technique

All the patients were operated in a supine position on a plain operation table either under regional or general anesthesia depending upon anesthetist's choice. No tourniquet was used. Pre-operatively all the patients were given a single shot of broad spectrum antibiotic through intravenous route. With the patient in the supine position (Figure 2), Fracture was reduced by applying the traction on the forearm and the assistant holding the humerus with elbow being in mild flexion. Reduction of the fracture was confirmed under image intensifier. After a satisfactory reduction a 1.5 mm wire was passed percutaneously through lateral epicondyle across the fracture and taking hold into the opposite cortex of the proximal fragment under image intensifier. Before inserting the medial wire through medial epicondyle following precautions were observed to minimize the risk of iatrogenic ulnar nerve injury:



**Figure 1: Pre-operative radiograph of the injured extremity (anteroposterior and lateral views) showing a Gartland Type III supracondylar fracture of the distal humerus**



**Figure 2: Patient positioning to reduce the extension type of supracondylar fracture of the humerus**

1. Elbow flexion was reduced to minimum desirable position
2. Small stab incision was given just behind the medial epicondyle to identify and secure ulnar nerve in few selected cases
3. Skin over the medial epicondyle was stretched posteriorly with the help of overlying fingers
4. The final position of fracture reduction and K-wires was verified under image intensifier. The extra length of K-wires was cut and tip of the remaining wires was bent (Figure 3) outside the skin. After K-wire fixation a posterior plaster of Paris (POP) splint was applied for 3 weeks in all the patients followed by a check X-ray immediately after the surgery (Figure 4).

### Post-operative Protocol

Intravenous analgesic and antibiotics were administered for the first 24 h after the surgery. A routine check radiograph including AP and lateral views of the operated elbow were done on the next morning in all the patients. On the next

day all the patients were switched to oral analgesics and antibiotics. Patients were routinely discharged on the second post-operative day.

**Follow-up and Outcome Assessment**

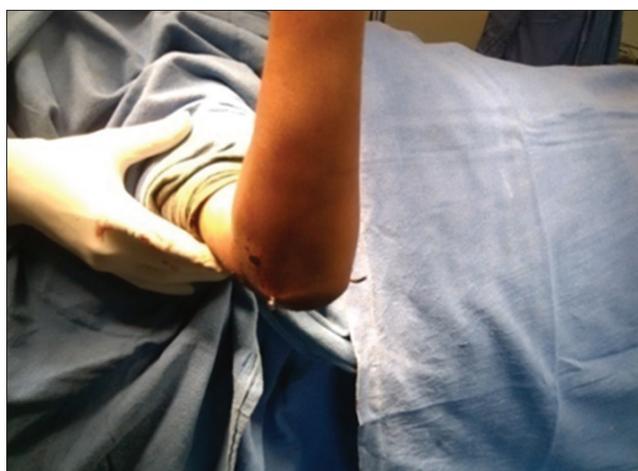
All the patients were called for routine follow-up in the outdoor department for clinico-radiological assessment of union and for any possible complication. Clinical union of



**Figure 4: Immediate post-operative radiographs (anteroposterior and lateral views) of the child showing anatomical reduction of the supracondylar fracture fixed with two cross Kirchner-wires**



**Figure 5: Four weeks follow-up radiograph (anteroposterior and lateral views) of the same patient showing union at the fracture site**



**Figure 3: Percutaneously inserted Kirchner-wires left outside the skin and bent at the ends**

the fracture was defined as the absence of tenderness at the fracture site and painless elbow motion. Radiological union was defined as the presence of bridging callus at the fracture site in both AP and lateral radiographs (Figure 5). After 3 weeks POP splint was removed in all the patients and elbow range motion were started. Removal of K-wires was done after confirmation of clinico-radiological union at the fracture site. Final assessment of the results was done according to Flynn’s criteria (Table 1).

**RESULTS**

There were 35 patients including 22 male and 13 female children. The mean age of the patient was 6.9 years (range 3-15 years). Union was observed in all the patients at a mean interval of 4.5 weeks (range 3-5 weeks). The peak incidence of the supracondylar fracture was found in children around the age of 7 years (Table 2).

Most (80%) of the injuries were the result of high velocity trauma including road traffic accidents and fall from

**Table 1: Flynn’s criteria**

Result	Rating	Functional outcome motion loss (°)	Cosmetic factor loss of carrying angle (°)
Satisfactory	Excellent	0-5	0-5
	Good	5-10	5-10
Unsatisfactory	Fair	10-15	10-15
	Poor	>15	>15

**Table 2: Age distribution of patient**

Age of patient (years)	Number of patients	Percentage
3-6	17	48.6
7-9	8	22.8
10-12	6	17.2
13-15	4	11.4
Total	35	100

**Table 3: Mode of injury**

Mode/mechanism of injury	Number of patient	Percentage
Road traffic accident	12	34.2
Fall from height/tree	16	45.8
Fall on the ground	7	20
Total	35	100

**Table 4: Fracture displacement**

Fracture displacement	Number of patients	Percentage
Gartland Type II	14	40
Gartland Type III	21	60
Total	35	100

height (Table 3). The majority (60%) of the fractures were Gartland Type III supracondylar fracture (Table 4).

Most common peripheral nerve injury observed was median nerve injury seen in 5 patients (Table 5), the next most common nerve involved was radial nerve seen in three patients. All these nerve injuries recovered following successful reduction and fixation of the fracture in a mean period of 10 weeks (range 6-14 weeks). One patient had presented with an established compartment syndrome following fracture (Table 5). This patient ultimately developed severe Volkmann ischemic contracture on subsequent follow-up.

One patient presented with a supracondylar fracture with gross posteromedial displacement, with well perfused but without a palpable radial artery in the injured upper extremity. This patient presented 24 h after sustaining the injury, an urgent reduction and fixation of the fracture was followed by the return of the peripheral pulses but, postoperatively this patient had mild ischemic contracture of the right forearm muscles. Three patients had an associated fracture of the distal end radius and ulna (Table 5).

The most common post-operative complication observed was a superficial pin tract infection seen in 5 (14.3%) patients (Table 6), this infection healed well following removal of infected pins and daily cleaning and dressing of the infected pin tracts supplemented by culture based oral antibiotics. None of the patient required hospitalization or intravenous antibiotics for pin tract infection. One patient had an iatrogenic ulnar nerve injury. Elbow stiffness was observed in 4 (11.4%) patients. Cubitus varus was seen in 1 patient, and implant loosening was seen in another 1 patient.

Overall based upon the Flynn's criteria 24 patients (68.6%) had excellent results, 6 (17.0%) patients had good, 3 (8.6%) had fair and 2 (5.8%) patients had poor functional results (Table 7).

## DISCUSSION

The most common pediatric fracture around the elbow in children <7 years of age is supracondylar fracture distal end humerus and with a male predominance. There are no controversies in the management of these fractures as far as the undisplaced fractures are concerned; such fractures can be successfully treated by immobilization alone with excellent results. The major controversy lies in the management of Gartland Type II and III displaced supracondylar fracture of the humerus. A variety of treatment options have been described for

**Table 5: Pre-operative complications see in patients**

Complication	Number of patients	Percentage
Established compartment syndrome	1	2.9
Pink pulse less hand	1	2.9
Radial nerve injury	3	8.6
Ulnar nerve injury	0	0.0
Median nerve injury	5	14.3
Open fracture	0	0.0
Associated fractures	3	8.6

**Table 6: Post-operative complications**

Complications	Number of patients	Percentage
Iatrogenic ulnar nerve injury	1	2.9
Iatrogenic median nerve injury	0	0.0
Pin tract infection	5	14.3
Loosening of K-wires	1	2.9
Malunion (varus)	1	2.9
Volk ischemic contracture	2	5.7
Elbow stiffness	4	11.4

K-wires: Kirchner-wires

**Table 7: Functional results based on Flynn's criteria**

Criteria	Number of patients	Percentage
Excellent	24	68.6
Good	6	17.0
Fair	3	8.6
Poor	2	5.8
Total	35	100

managing displaced supracondylar fractures ranging from conservative treatment on traction to close or open reduction and internal fixation using different configuration of pins/K-wires with each method having its own merits and demerits.<sup>13-18</sup>

Two most common configurations of the K-wires for fixation of the pediatric supracondylar fracture of humerus are cross K-wire configuration and lateral K-wire configuration in parallel or divergent fashion with its advantages and disadvantages. The major disadvantage of cross K-wire configuration is the risk of iatrogenic ulnar nerve injury however, it said to biomechanically the strongest construct. The major advantage of lateral K-wire placement is that it is free from the risk of an iatrogenic ulnar nerve injury. In our study only 1 (2.9%) patient had an iatrogenic ulnar nerve injury. Some authors have advocated the use of ultrasound to minimize the risk of ulnar nerve injury during insertion of medial pin; however, it is technically demanding, and the expertise may not be available easily.<sup>19</sup> Although the risk of iatrogenic peripheral nerve injuries following supracondylar fracture of the humerus has been reported ranging from 2% to

6% in various in various studies, in our study we observed this complication in only 2.9% patients, and this injury recovered at 6 months follow-up.<sup>20,21</sup>

The other poor indicator of treatment of supracondylar fracture of the humerus is the cubitus varus deformity due to residual medial tilt and rotation of the distal fragment. In present study one (2.9%) patient had cubitus varus deformity. The other major complication observed in the present study was superficial pin tract infection seen in 5 (14.3%) patients. This infection was managed successfully in all the patients without the need of patient readmission or parental antibiotics. Elbow stiffness was encountered in 4 (11.4%) patients in the present study; two of these patients had only fair results based on Flynn's criteria. Pin loosening was seen in one patient following accidental removal of POP splint during follow-up visit of the patient.

Two patients with vascular complications had poor results based on Flynn's criteria. In one patient who presented with a full blown compartment syndrome of the forearm, even after urgent management of the fracture the patient developed Volkmann ischemic contracture. Another patient who presented with grossly displaced supracondylar fracture with an absent radial artery pulsation, an urgent reduction and fixation of the fracture lead to return of peripheral arterial pulsations in the injured extremity, but on subsequent follow-ups the patient showed signs of mild muscle ischemia. Based on Flynn's criteria 85.6% patients in our study had God to excellent results, 8.6% patients had fair results and only 5.8% patients had poor results.

## CONCLUSION

Closed reduction and medial-lateral percutaneous K-wire fixation is the treatment of choice for displaced pediatric supracondylar fractures of the humerus with an acceptably low risk of iatrogenic ulnar nerve injury.

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# Immunological Response of Human Immunodeficiency Virus Positive Patients after Initiation of Highly Active Antiretroviral Therapy

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## Abstract

**Background:** Effective care for people living with human immunodeficiency virus (PLHIV) requires highly active antiretroviral therapy (HAART). HAART mainly acts on suppression of viral replication and allows the recovery of patient's immune system protecting him/her from the development of AIDS and death.

**Objective:** The study aims to document the experience of immunological response among PLHIV on HAART comparing different categories of patients.

**Methods:** This is a retrospective analytical quantitative study with a sample size of 224 patients who were started with HAART. A total of three CD4 counts were measured pre-therapy, 1st post therapy, and 2nd post therapy at 6 monthly intervals to determine the change in CD4 counts. The rates of CD4 change were also compared among the different categories of patients.

**Results:** Men had higher CD4 count (mean of 96.4 cells) with mean age of participants being 37 years at baseline. The CD4 count increased from a mean baseline of 86.2 cells to 372.2, 390.0, respectively, at 6, 12, months of treatment ( $P < 0.001$  at each time point). There was no gender ( $P = 0.46$ ) and age ( $P = 0.96$ ) differences in treatment response. There was no much difference ( $P = 0.18$ ) in treatment response comparing those with CD4  $< 200$  and those with CD4 count  $> 200$  at baseline although patients with baseline CD4 count  $< 200$  cells showed larger increases after 12 months of treatment. The patients with pre-therapy CD4 count  $< 200$  cells, 127 (81.4%) patients out of 156 were adherent, and 29 (18.6%) were non-adherents.

**Conclusion:** Adherent patients with base line CD4  $< 200$  achieved greater improvement in their CD4 cell counts. A high level of adherence to HAART is required to achieve a significant improvement in CD4 cell counts (immunological improvement) among PLHIV.

**Key words:** Human immunodeficiency virus, Immunological, Patient, Therapy

## INTRODUCTION

Since its discovery in 1981 by Centers for Disease Control in the US, human immunodeficiency virus (HIV) became an emerging disease and became a global pandemic. Approximately, 35.3 million people have HIV world wide<sup>1</sup> with 2.3 million people infected newly in 2012 and are down from 3.1 million new infections in 2001. It resulted in

1.34 million deaths in 2013, down from a peak of 2.2 million in 2005.<sup>2</sup> In India, as of 2013 estimates 2.1 million people living with HIV (PLHIV). As per NACO report 1.16 lakh new infections in 2011 and PLHIV is estimated as 2.1 million and AIDS-related deaths being 1.48 lakhs.<sup>3</sup>

Effective care for PLHIV requires highly active antiretroviral therapy (HAART) for those who are eligible for treatment.<sup>4</sup> Mortality and morbidity rates in HIV-infected individuals in countries with widespread access to HAART have been decreased. HAART mainly acts on suppression of viral replication and allows the recovery of patient's immune system protecting him/her from the development of AIDS and death. In developing countries, viral load is not done due to several limitations and initiation of ART depends on clinical and immunological assessment.<sup>5</sup>

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The immunological response of PLHIV initiated on HAART in our region is not well documented, but there is documentary evidence on immunological response to HAART is well documented.<sup>5,6,7</sup> The study objective, therefore, was to document the experience of immunological response among PLHIV on HAART in our region comparing different categories of patients.

## METHODS

The study was conducted between January 2014 and December 2014. HAART was initiated in population with baseline CD4 <350 cells. These patients were stratified into two CD4 categories: The patients with CD4 cell count <200 cells and those CD4 cell count >200 cells. HAART regimen consists of two nucleoside reverse transcriptase inhibitors (NRTIs) and one non-NRTIs.<sup>6</sup> “Adherent” was defined as patients with >95% drug intake without interruptions while “non-adherent” was defined as patients who defaulted in treatment during the study period. Adherence was monitored using pharma fill cards.<sup>8,9</sup>

The study population composed of HIV-positive patients, who were treatment naïve. These patients had enrolled at the Rajiv Gandhi Institute of Medical Sciences and were due to start HAART treatment. The patients’ demographic data and clinical data collected from their clinic files. The total sample size was 224. Three CD4 count measurements were taken at 6 monthly intervals. These were pre-therapy, 1<sup>st</sup> post therapy, and 2<sup>nd</sup> post therapy counts.

Univariate analysis was done to determine the association between treatment response and age of the patient. For all comparisons, *P*-value was taken as *P* < 0.05 for establishing statistical significance.

## RESULTS

The geometric mean of CD4 counts was taken. Of the 224 patients in the study, 198 (88.3%) were adherents. Of these 198 patients, 127 (56.6%) patients had their baseline CD4 cell count <200. Remaining 26 (13.5%) patients were non-adherents. The main baseline characteristics are shown below in Table 1. The following table shows the age, gender distribution of population, their level of education and economic status.

The patients were divided into three groups based on their age. 156 adherent patients with their baseline CD4 cell count of <200 were evaluated for immune response to HAART after 6, 12 months of treatment (Table 2). The mean pre-therapy CD4 cell count was 86.22 cells. A significant response to treatment occurred after 6 months of therapy

with a mean CD4 increase to 372 cells (*P* < 0.001). Subsequently, a slower steady increase in CD4 counts is observed as shown in Figure 1. The immunological response to HAART was very much significant in the first 6 months of treatment (from 86.22 to 372 cells) with *P* < 0.001.

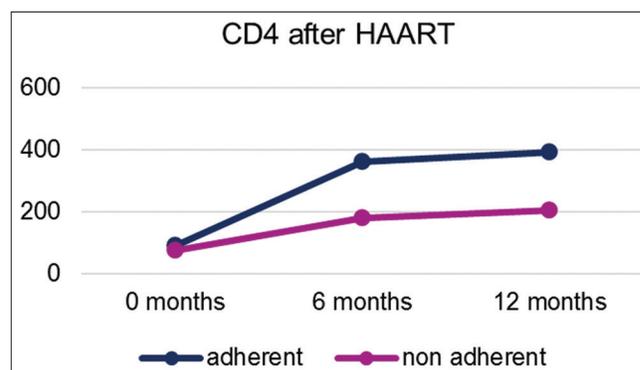
In all, there were 156 patients who started therapy with baseline CD4 count of <200 cells. Of this, 127 (81.4%) and 29 (18.6%) were adherents and non-adherents respectively

**Table 1: Baseline characteristics**

Characteristics	n (%)
Gender	
Women	101 (45.1)
Men	123 (54.9)
Employment status	
Unemployed	20 (8.9)
Self-employed	106 (47.3)
Workers	58 (25.8)
Missing data	40 (17.8)
Level of education	
Non-educated	36 (13.7)
Primary/JSS	127 (48.5)
Secondary	36 (13.7)
Tertiary	15 (5.8)
Missing data	48 (18.3)
Age group (years)	
<12	4 (0.1)
12-60	208 (92.8)
>60	12 (5.3)

**Table 2: Age-wise and gender-wise distribution with their geometric mean of baseline CD4**

Characteristics	Baseline CD4 (cells/\$I)
Age (years)	
<12	68.7
12-60	87.6
>60	86.9
Sex	
Women	89.6
Men	96.4

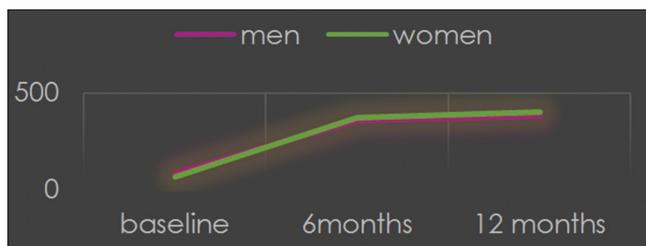


**Figure 1: Rate of CD4 increases showing immunological response of 156 patients who commenced therapy with baseline count of <200 cells**

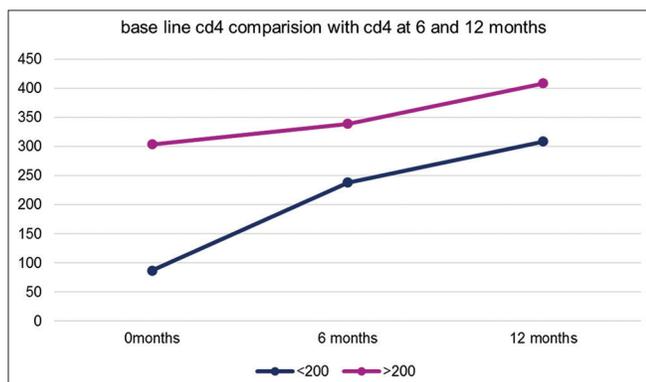
The immune responses of these both adherents and non-adherents (both of which had baseline CD4 count <200 cells) were compared. The mean pre-therapy CD4 count for adherent patients was 89 which were slightly higher than non-adherent patients (89 cells) as shown in Figure 2. After 6 months of treatment, CD4 count had increased to 362 ( $P < 0.001$ ) and 180 cells ( $P = 0.21$ ) for adherents and non-adherents, respectively.

Among the adherent patients in the study, there were a higher proportion of men (65.2) than women (34.8). Men exhibited higher CD4 count values (84.6 cells) than women (67.8 cells) before therapy. The rise in CD4 count for men and women were 360.8 and 374.2 cells at 6 months, and 384.2 and 402.6 at 12 months. A univariate analysis was done for the patient's counts, and it showed significant improvement in CD4 for both men and women, respectively. However, no significant gender difference in treatment response ( $P = 0.35$ ) after 12 months was found.

Adherent patients were divided into two categories: Baseline CD4 count of <200 and baseline CD4 count between >200. Mean pre-therapy CD4 count was 57.8 and 303.4 cells. CD4 counts came as 238.1 cells and 308.6 cells at 6 and 12 months, respectively, for those with CD4 <200, and 339.8 cells and 408.6 cells for CD4 >200. Figure 3 shows the relation between the baseline CD4 and treatment response.



**Figure 2: The relation between men and women with their CD4 differences**



**Figure 3: The relation between the baseline CD4 and treatment response**

## DISCUSSION

This study showed immunological recovery in two phases. A rapid phase of improvement within 6 months of therapy with a mean of 372 cells followed by more gradual second phase improvement with a mean of 390 cells at 12 months. The rapid early rise in CD4 counts in the first 6 months after HAART therapy is due to reconstitution and redistribution of CD4T cells into circulation from the lymph nodes where they were sequestered.<sup>10</sup> Touloumi *et al.*<sup>11</sup> described that slower increase in the second phase is due to the production of new CD4 cells which takes a long time.

A high level of adherence is observed in most patients in our study. Similar adherence rates were observed in a study in Cambodia where as high as 95% patients were seen.<sup>12</sup> Non-adherent patients were started treatment with a slightly higher baseline CD4 count than adherent patients. However, adherent patients showed a significant rise in CD4 ( $P < 0.01$ ), whereas non-adherent patients recorded insignificant rise in CD4 ( $P = 0.21$  and  $0.48$  at 6 and 12 months, respectively). Rougemont *et al.*<sup>13</sup> credits adherence as a major key for attaining good immunological improvement.

Higher proportion of men demonstrating higher CD4 count (96.4 cells) than woman (89.6 cells) at baseline. Good immunological recovery was observed during therapy in both sexes. No gender difference was found in treatment response ( $P = 0.46$ ). The study showed that better response was observed in younger and middle-aged patients. This is attributed to preserved thymic function in young people. The slower immune response in older age is due to the gradual deterioration of the immune system as a result of the functional decline of T cells with age. Age of patient at the start of HAART therapy could influence CD4 cell recovery. The study depicted that patients with lower CD4 counts showed significant rise at 6 and 12 months, respectively. Many studies reported greater CD4 increases among highly advanced adherent patients as in our study. A study<sup>14</sup> in Botswana reported significant increase after 4 weeks of treatment in patients with <200 cells. The study results cannot be generalized as small study population makes a major limitation.

## CONCLUSION

Significant immunological recovery is seen among PLHIV on HAART with a high level of treatment adherence. Significant CD4 improvement is seen with in the first 6 months of treatment in patients started on HAART therapy with baseline CD4 count <200. Adherence can

be used as an indicator for HIV drug resistance and monitoring

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# Comparative Study of Onlay and Pre-Peritoneal Mesh Repair in the Management of Ventral Hernias

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## Abstract

**Background:** A ventral hernia in the anterior abdominal wall includes both spontaneous and incisional hernias after an abdominal operation. Mesh repair can be onlay or pre-peritoneal. Controversy exists regarding the use of the type of either meshplasty, due to differences in ease in performing the surgery, time of surgery, complications occurring in the post-operative period and the recurrence.

**Aims:** (1) To study the anatomical, etiological and clinico-pathological factors leading to ventral hernias. (2) To study the different techniques of repair of ventral hernia with emphasis on pre-peritoneal and onlay mesh repair and their outcomes.

**Materials and Methods:** 60 patients presenting with the ventral hernias were admitted to Mahatma Gandhi Memorial Hospital, Warangal, from August 2012 to September 2013 and were preoperatively assessed clinically and by ultrasonography to confirm the diagnosis. 30 patients each underwent pre-peritoneal and onlay mesh repair after obtaining consent and satisfying the inclusion and exclusion criteria.

**Results:** Seroma formation, infection, and chronic pain were seen in 20%, 13.33%, 20% patients, respectively, in onlay mesh repair group and in 10%, 6.66%, and 3.33% patients, respectively, in pre-peritoneal mesh repair group. Recurrence was seen in 10% patients in onlay group. No recurrence was seen in the pre-peritoneal mesh repair group. Associated factors' morbidity was also found to be higher in onlay group.

**Conclusion:** Seroma formation, infection, and the chronic pain were commonly associated with onlay mesh repair compared to pre-peritoneal mesh repair. Recurrence is higher in cases of ventral hernias operated by onlay mesh repair especially in cases with co-morbidities such as obesity, diabetes, and multiparity. Considering all these observations, we concluded that pre-peritoneal mesh repair is superior to onlay mesh repair.

**Key words:** Incisional hernia, Mesh repair, Onlay, Pre-peritoneal, Recurrence

## INTRODUCTION

Ventral hernia is a protrusion of an abdominal viscus or part of a viscus through the anterior abdominal wall occurring at any site other than the groin. It includes

incisional hernias, paraumbilical hernias, umbilical hernia, epigastric hernias, and spigelian hernias, respectively.<sup>1</sup>

The patient seeks medical advice for swelling, discomfort, acute pain, associated gastrointestinal symptoms, or cosmetic symptoms. Diagnosis can be achieved with ease by clinical examination or by ultrasound scanning.

### Etiology

The formation of ventral hernias is a multifactorial and complex process. Three types of ventral hernias are recognized: Spontaneous, congenital, and incisional hernias. In 90% of patients, it is an acquired defect

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that is a direct result of increased abdominal pressure.<sup>2</sup> Causes of this increase in abdominal pressure include multiparous status, obesity, and cirrhosis with ascites.<sup>3</sup> Numerous patient-related factors may lead to the formation of ventral hernias and include obesity,<sup>4</sup> older age, male gender,<sup>5</sup> sleep apnea,<sup>4</sup> emphysema and other chronic lung conditions, prostatism,<sup>6</sup> abdominal distention, steroids,<sup>6</sup> and jaundice,<sup>7,8</sup> although some of these causes are controversial. Some evidence suggests that certain biochemical processes, including the metalloproteinases, may lead to both aneurysmal disease and hernia formation. These collagen defects have also been implicated in a higher rate of incisional hernia formation after aortic surgery.<sup>9</sup> The concept of “metastatic emphysema,” that is, the same processes that break down pulmonary tissue disturb normal fascia, was introduced by Dr. Raymond Read and appears to be well founded.<sup>10</sup>

Incisional hernias are unique in that they are the only abdominal wall hernias that are considered to be iatrogenic. It continues to be one of the more common complications of abdominal surgical procedures and is a significant source of morbidity and loss of time from productive employment. Studies have shown that transverse incisions are associated with a reduced incidence of incisional hernia compared to midline vertical laparotomies, although the data are far from conclusive.<sup>11,12</sup>

### Operative Management of Ventral Hernias<sup>13-17</sup>

For many years, the repair of incisional hernia was associated with a high recurrence rate. In more recent years, the introduction of synthetic prosthetic materials has provided the opportunity to perform a tension free repair, thereby reducing the rate of recurrence.

#### Indications

1. Pain and discomfort
2. Large hernias with small openings
3. A history of recurrent attacks of subacute obstruction, incarceration, irreducibility, and strangulation
4. For cosmetic reasons for a large and unsightly hernia.

#### General Principles in Repair of Ventral Hernias

1. Spinal and epidural anesthesia gives excellent relaxation with minimal respiratory depression
2. Hemostasis should be as careful and as effective as possible
3. Non absorbable suture material should be used for the repair
4. The choice of incision is governed by the orientation of the defect
5. Healthy fascia must be isolated
6. Closure of the sac is done in one layer, incorporating both fascia and peritoneum after opening the sac,

freeing all adhesions, reducing the viscera and exploring the abdomen

7. Drains should be used wherever needed.

#### Operative Methods for Repair of Ventral Hernia

The three basic methods are:

1. Primary suture or edge to edge closure
2. Shoelace darns repair
3. Synthetic non-absorbable mesh closure

The method chosen depends on the size of the hernial defect. The size of hernia can be assessed with the patient standing and coughing. The size of the defect and its behavior can be examined with the patient supine. The surgeon's hand with fingers straightened is inserted into the defect, and the patient is requested to raise his head and shoulders forward without the aid of his hands. If necessary, he is asked to raise his straightened legs at the same time.

The repair of narrow hernias is by shoelace technique. This is a quick, easy, and extra peritoneal method that simply returns the unopened hernial sac and its contents to the abdominal cavity and then avoids the tedious and perhaps risky dissection of the adherent loops of bowel on the inner surface of the sac and abdomen. Since the defect is narrow, the lateral cut edges of the rectus sheath come together in the midline and are anchored to the new linea alba. Hernias with a wider defect also can be conveniently repaired by the shoelace darn technique. The third method for these hernias involves the use of sheets of woven or knitted mesh of synthetic non-absorbable materials such as polypropylene, polyester or sheets of expanded polytetrafluoroethylene (PTFE) placed across the defect and stitched to the abdominal wall.

The most common and most favored material today is knitted polypropylene. This method of repair of large post-operative ventral abdominal hernias is a good one and has undoubtedly become popular. It may involve the resection of the hernial sac and the dissection of the adherent loops of bowel with the risk of fistula formation. A large foreign body is used, and the procedure is timeconsuming and requires prolonged anesthesia, whereas shoelace technique is simple, quick, and entirely extra peritoneal.

#### Prosthetic Mesh Repair

##### Material of choice

The ideal mesh is one that is cheap and universally available, is easily cut to the required shape, is flexible, slightly elastic, and pleasant to handle. It should be practically indestructible and capable of being rapidly fixed and incorporated by human tissues. It must be inert and elicit little tissue reaction. It must be sterilisable and non-carcinogenic. Polypropylene mesh meets the requirements

of the ideal prosthesis and is today the most common used material for repair of all types of hernia.

**The other prosthetic meshes tried are PTFE (Teflon, Gore-Tex), polyester mesh (Dacron), polyglycolic mesh, polyglactic mesh, metal meshes, and gelatin film.**

#### *Indications for mesh repair*

The indications are:

- a. Repair of recurrent incisional hernias: Successful repair of recurrent hernias in patients, whose musculature is of poor quality and weak and flabby, fascial coverings are thin and weak, requires prosthetic material.
- b. In the primary repair of a massive hernia in which tissues are deficient and repair without tension cannot be accomplished readily by conventional techniques of direct suturing. The employment of a bridging prosthesis in a massive incisional hernia will enable the surgeon to avoid excessive tension in wound closure and the hazards of increased intra-abdominal pressure.
- c. When continued presence of forces tending to disrupt in the future is reasonably predictable. There are certain conditions which present a relatively high risk of recurrence unless prosthetic materials are used. They are chronic cough, increased intra-abdominal pressure from obesity, and massive incisional hernias.
- d. Losses of essential fascial segments by severe trauma, radical resection of malignant tumors involving the abdominal wall may sometimes require prosthetic materials for effective closure.

#### **Types of Mesh Repair**

Various techniques of prosthetic mesh implantation have been explained.

#### *Onlay technique*

In this technique, after managing hernial sac and its contents, aponeurosis is approximated using polypropylene suture and the prosthetic mesh is placed over the aponeurosis and fixed with polypropylene suture material.

#### *Inlay mesh repair*

After reducing the sac and its contents, the peritoneum is closed using chromic catgut and mesh fixed with polypropylene suture material. Rectus sheath is closed over the mesh. Suction drain kept and wound closed in layers. When placed in the pre-peritoneal position in complex ventral hernia repairs, complication rates are low<sup>18,19</sup>

#### *Intraperitoneal underlay mesh repair*

This technique allows for the largest underlay of mesh on the fascia or abdominal wall, which should reduce recurrence because a larger amount of tissue in growth can occur, reducing possible mesh fascia separation. The open technique involves opening the hernial sac, dissecting

bowel away from the abdominal wall, and placing the mesh intraperitoneally with the non-adhesive surface of mesh facing against the abdominal contents and the tissue in growth side of the mesh against the muscular or fascial side of the abdominal wall. Fixation of the mesh material is currently being debated among surgeons.

#### **Laparoscopic Repair of Ventral Hernia**

The laparoscopic approach involves entering the abdomen away from the hernia defect, lysing adhesion to remove structures from the hernial sac, and adjacent abdominal wall. The mesh is inserted through a trocar site and fixed to the abdominal wall with partial thickness tacks or full thickness abdominal muscular or fascial wall suture. The latter is more technically challenging but also more closely duplicates the open approach. The laparoscopic approach has been noted to have a significant seroma rate of approximately 10-15%. The recurrence rates have generally been <5%.<sup>20</sup>

## **MATERIALS AND METHODS**

60 patients presenting with ventral hernia admitted to Mahatma Gandhi Memorial Hospital, Warangal, from August 2012 to September 2013 were preoperatively assessed clinically and by ultrasonography to confirm the diagnosis. 30 patients each underwent pre-peritoneal and onlay mesh repair after obtaining consent and satisfying the inclusion and exclusion criteria. Statistical significance was confirmed using SPSS 11.1 software.

#### **Inclusion Criteria**

All patients presenting with anterior abdominal wall hernias:

- a. Umbilical hernias
- b. Epigastric hernias
- c. Paraumbilical hernias
- d. Incisional hernias.
- e. Spigelian hernias

#### **Exclusion Criteria**

- a. Groin hernia
- b. Divarication of recti
- c. Patients <12 years of age
- d. Patients medically not fit for surgery.

#### **Follow-up**

All the patients were regularly followed up for 12 months.

## **RESULTS**

#### **Percentage Distribution of Ventral Hernias**

In this study of 60 patients of ventral hernia, the most common type of ventral hernia was incisional hernia (40%). Epigastric hernia was the least common type (11.7%) (Table 1).

### Age Distribution

The total number of cases studied was 60. The study showed that the maximum number of patients were in the 4<sup>th</sup> decade of life (58.3%). There were no patients in the age groups 0-10 and 11-20 (Table 2).

### Sex Distribution

In a total of 60 cases, 42 patients (70%) were females, and 18 patients (30%) were males (Table 3).

### Type of Previous Operation in Incisional Hernia

In our study in cases with incisional hernia (24), 12 cases (50%) underwent tubectomy, 11 lower segment caesarian section (LSCS) (45.8%), and 1 patient underwent hysterectomy (4.2%) (Table 4).

### Mode of Presentation

Most of the patients, 51 (85%) presented with swelling, 7 (11.66%) with pain and swelling, and 2 patients with pain, swelling, and vomiting (Table 5).

**Table 1: The ventral hernias with respect to number and percentage**

Type of hernia	Number	Percentage
Incisional	24	40
Paraumbilical	18	30
Umbilical	11	18.3
Epigastric	7	11.7
Total	60	100

**Table 2: Age distribution**

Age in years	Number of cases	Percentage
0-10	0	0
11-20	0	0
21-30	9	15
31-40	35	58.3
41-50	13	21.7
51-60	3	5

**Table 3: Sex distribution**

Sex	Number of patients	Percentage
Male	18	30
Female	42	70

**Table 4: Types of previous operations in incisional hernia**

Previous operation	Number of patients	Percentage
Tubectomy	12	50
LSCS	11	45.8
Hysterectomy	1	4.2

LSCS: Lower segment cesarian section

### Associated Risk Factors or Illness

Of the 60 patients, 15 (25%) were obese, 8 (13.33%) were diabetic, 1 (1.67%) was anemic, and one (1.67%) was hypothyroid. Hence, obesity was the most common associated risk factor (Table 6).

### Size of the Defect

The smallest defect measured was 2 cm × 2 cm and the largest defect measured 6 cm × 6 cm in this study.

### Antibiotic

All patients were given a dose of third generation cephalosporin at the time of induction of anesthesia, continued with intravenous antibiotics post operatively.

### Content of the sac

50 (83.34%) patients had omentum as the content of the sac. 5 (8.33%) had jejunum, 4 (6.66%) had ileum, and 1 (1.67%) had a transverse colon. Hence, omentum was the most common content of the hernial sac (Table 7).

### Type of Mesh Repair

30 (50%) patients underwent pre-peritoneal mesh repair, and 30 (50%) patients underwent onlay mesh repair (Table 8).

**Table 5: Symptoms/mode of presentation**

Symptoms	Number of cases	Percentage
Swelling	51	85
Swelling and pain	7	11.67
Swelling, pain, and vomiting	2	3.33

**Table 6: Associated risk factors/illness**

Condition	Number of patients	Percentage
Obesity	15	25
Diabetes	8	13.33
Anemia	1	1.67
Hypothyroidism	1	1.67

**Table 7: Contents of the sac**

Content of the sac	Number of patients	Percentage
Omentum	50	83.34
Jejunum	5	8.33
Ileum	4	6.66
Transverse colon	1	1.67

**Table 8: Types of mesh repair**

Type of mesh repair	Number of patients	Percentage
Pre-peritoneal mesh repair	30	50
Onlay mesh repair	30	50

### Duration of surgery

Mean duration of surgery in Onlay Mesh repair was 45 min and that in pre-peritoneal Mesh repair was 60.15 min.  $P < 0.0001$  (Table 9).

### Post-operative Complications

Seroma was the most common complication followed by chronic pain and wound infection. Seroma was drained. Chronic pain was managed with analgesics and reassurance. Wound infection was treated with antibiotics and regular dressings (Table 10).

### Follow-up and Recurrence

All the patients were regularly followed up for 1 year. Recurrence was observed only in patients with onlay mesh repair. 4 (13.33%) patients out of 30 patients who underwent onlay mesh repair had a recurrence (Table 11).

## DISCUSSION

Ventral hernias in the anterior abdominal wall include both spontaneous and most commonly, incisional hernias after an abdominal operation. It is estimated that 2-10% of all abdominal operations result in an incisional hernia.

Small hernias  $<2\frac{1}{2}$  cm in diameter are often successfully closed with primary tissue repairs. However, larger ones have a recurrence rate of up to 30-40% when a tissue repair alone is performed.<sup>14</sup> Hernia recurrence is distressing to patient and embarrassing to surgeons. Nowadays tension free repair using prosthetic mesh has decreased recurrence to negligible. Despite excellent results increased the risk of infection with the placement of a foreign body and cost factor still exist; however, operating time and hospital length of stay are shortened. Primary tissue repair is associated with higher unacceptable recurrence rate, nowadays; tension free mesh repair is ideal hernia repair technique.<sup>15</sup>

Mesh repair can be pre-peritoneal or onlay. Controversy exists among the surgeons regarding the use of a type of either mesh repair, due to differences in ease in performing the surgery, time of surgery, complications occurring in the post-operative period and the recurrence. In our study, attempt has been made to study both types of these mesh repair and their outcome.

### Incidence

Incidence among ventral hernias was Incisional hernia - 40%, paraumbilical hernia - 30%, umbilical hernia - 18.3%, epigastric hernia - 11.7%.

### Age

Ventral hernias are more common in patients aged between 30 and 40 years (58.3%) in our study. Youngest patient in

our study was 25-year-old. It was found that ventral hernias are rare after 60 years as no patient was more than 60 years in our study.

### Sex

Ventral hernias are more common among females. 42 patients were females, and 18 patients were male. In literature, the ratio is 3:1 but in our study, it is 2.33:1. There is no significance difference in the age distribution in males and females, as disease is more common between 30 and 40 years in both. Ellis *et al.*<sup>13</sup> have obtained a 64.6% of female population in the study of 342 patients. In our study, female population was 70% while Godara *et al.*<sup>21</sup> series had a female population of 42.5% (Table 12).

### Associated Factors in Incisional Hernia

Among incisional hernias gynecological surgeries are the most common associated surgeries. Tubectomy was the most common predisposing surgery, constituting 50% followed by LSCS (45.8%) and hysterectomy (4.2%). Godara *et al.* series<sup>21</sup> also mentions gynecological surgeries as the most common associated surgery.

### Associated Factors with Ventral Hernias

In females most precipitating factor was multiparity. Out of 42 patients, 21 (50%) were multipara. This can be attributed

**Table 9: Duration of surgery**

Type of mesh repair	Mean duration of surgery (min)
Onlay	45
Pre-peritoneal	60.15

**Table 10: Post-operative complications**

Complication	Pre-peritoneal	Onlay	Pre-peritoneal (%)	Onlay (%)	P value
Seroma	3	6	10	20	0.3
Wound infection	2	4	6.66	13.33	0.4
Mesh infection	0	0	0	0	-
Chronic pain	1	6	3.33	20	<0.05
Intestinal fistula	0	0	0	0	-

**Table 11: Recurrence percentage**

Type of operation	Recurrence	Percentage	P value
Pre-peritoneal mesh repair	0	0	-
Onlay mesh repair	4	13.33	<0.04

**Table 12: Female percentage**

Study group	Percentage females
Ellis <i>et al.</i> <sup>13</sup>	64.6
Godara <i>et al.</i> <sup>21</sup>	42.5
Present study	70

to stretching and weakening of anterior abdominal wall musculo-aponeurotic layer. Next common factor was obesity-15 patients (25%). Fat penetrates muscle bundles and layers, weakens aponeurosis and favors appearance of hernia. 8 (13.33%) patients were diabetic, 1 (1.67%) was anemic, and 1 (1.67%) was hypothyroid. In the present series, post-operative morbidity was considerably high in diabetics, contributing 80% of the cases which had post-operative wound infection in the post-operative period. Obesity was another factor that led to increased post-operative morbidity with all 9 cases, of 60 cases in the present series, who developed one or the other post-operative complications being obese. These two important factors are compared with series published by Rios *et al.* and Weber *et al.* in Table 13. Results in the present series are comparable to both these studies.

**Clinical Presentation**

All patients presented with swelling. About seven patients had pain in the swelling or dragging type of pain abdomen. One patient with incisional hernia and one with umbilical hernia presented with signs of intestinal obstruction and were operated immediately to reduce the hernia and the defect repaired by onlay mesh repair. Toms *et al.*<sup>22</sup> concluded that abdominal hernias can present asymptotically to life treating emergencies. About 51 (85%) cases were without complications, 7 (11.67%) were irreducible, and 2 (3.33%) were obstructed. No strangulated case was observed.

**Contents of the Sac**

The commonest content of the sac observed was omentum 50 (83.33%), followed by jejunum 5 (8.33%), ileum 4 (6.66%), and transverse colon was found in one case (1.67%).

**Mean Duration of Surgery**

Mean duration of surgery in our series, in cases that underwent onlay mesh repair was 45 min, while in cases with pre-peritoneal Mesh repair took more time and the duration of surgery was 60.15 min in present series ( $P < 0.0001$ ). The difference could be accounted to more time required for dissection for creating pre-peritoneal space. Securing adequate hemostasis is another burden on time. Ease of operation was largely subjective and depends on surgeons' experience, exposure, quality of assistance, and conductive facilities. Godara *et al.*, reported a mean duration of 49.35 min for onlay and a mean duration of 63.15 min for pre-peritoneal mesh repair ( $P < 0.0001$ ), while in Gleysteen<sup>23</sup> series the mean duration for onlay and pre-peritoneal mesh repair were 42 and 70.5 min, respectively. Table 14 shows the comparison of duration of surgery in different series.

**Complications**

The most common complication observed was seroma in 9 patients (15%). Out of 9 patients, 3 (10%) were in pre-

peritoneal and 6 (20%) in onlay mesh repair group. This complication was managed with seroma drainage. Onlay technique had more of seroma formation, due to the fact that onlay techniques require significant subcutaneous dissection to place the mesh, which can lead to devitalized tissue with seroma formation or infection. The superficial location of the mesh also puts it in danger of becoming infected if there is a superficial wound infection.

Wound infection was found in 6 cases (10%). Out of these, 2 (6.66%) were in a pre-peritoneal group and 4 (13.33%) were in onlay group. These patients were treated with appropriate antibiotics and regular dressing. No patient required removal of mesh because the infection was superficial and responded well to antibiotics.

Chronic pain was a complaint of 7 patients (11.6%) in all. Out of these 6 (20%) were in onlay group while one (3.33%) in pre-peritoneal mesh repair group ( $P < 0.05$ ). The reason for chronic pain in Onlay Mesh repair may be because mesh is placed below subcutaneous plane over the muscle and sutured over it that causes chronic muscle irritation and because of the fact that the closure is in tension.

A significant difference was noticed in chronic pain, between the two techniques, based on the  $P$  value calculated on SPSS Software 11.1 while the other complications were comparable between both types of mesh repairs (Table 15).

**Hospital Stay**

The duration of post-operative hospital stay is an indirect indication of the degree of morbidity in terms of post-operative complications. Average post-operative hospital

**Table 13: Associated factors with ventral hernias**

Study group	Diabetes	Obesity (%)
Rios <i>et al.</i>	18	9.3
Weber <i>et al.</i>	23	30
Present study	13.33	25

**Table 14: Mean duration of surgery**

Mean duration in minutes (%)	Godara <i>et al.</i> <sup>21</sup> (100)	Gleysteen <sup>23</sup> (125)	Present study (*50)
Onlay	49.35	42	45
Pre-peritoneal	63.15	70.5	60.15

**Table 15: Post-operative complications**

Complications* (%)	Godara <i>et al.</i> <sup>21</sup>	Gleysteen <sup>23</sup>	Present study
Onlay	15	19	20
Pre-peritoneal	22.5	12	10

\*Includes seroma, wound infections, and chronic pain

stay period in present series for onlay mesh repair was 7.53 days, as compared to 5.96 days average hospital stay for pre-peritoneal mesh repair ( $P < 0.0002$ ), which were comparable to series published by de Vries Reilingh *et al.*<sup>24</sup> and Gleysteen<sup>23</sup> Comparative results are shown in Table 16.

### Recurrence

No recurrence of hernia was noticed in pre-peritoneal mesh repair; in present series where as in the onlay group recurrence occurred in 4 (13.33%) cases ( $P < 0.04$ ). Gleysteen<sup>23</sup> found a recurrence rate to be 20% in onlay and 4% in pre-peritoneal mesh repairs (Table 17). A retrospective study in Europe done by de Vries Reilingh *et al.*<sup>24</sup> noticed a recurrence rate of 23% in cases that underwent onlay mesh repair, and no recurrence in patients with pre-peritoneal mesh repair.

Pre-peritoneal mesh repair is considered superior because the mesh with significant overlap placed under the muscular abdominal wall works according to Pascal's principles of hydrostatics. The intra-abdominal cavity functions as a cylinder, and, therefore, the pressure is distributed uniformly to all aspects of the system. Consequently, the same forces that are attempting to push the mesh through hernia defects are also holding the mesh in place against the intact abdominal wall. In this manner, the prosthetic mesh is held firmly in place by intra-abdominal pressure. The mechanical strength of the prosthetic mesh prevents protrusion of the peritoneal cavity through the hernia because the hernial sac is indistensible against the mesh. Over time, the prosthetic mesh is incorporated into the fascia and unites the abdominal wall, now without an area of weakness.

### CONCLUSION

1. In the patients presenting with ventral hernia, it is important to recognize the associated risk factors such as diabetes, obesity, parity, previous surgeries to carefully plan the type of repair either pre-peritoneal

or onlay repair to prevent the complications such as seroma formation, wound infection, chronic pain, and the recurrence.

2. Seroma formation, infection, and the chronic pain are found to be more commonly associated with onlay mesh repair compared to pre-peritoneal mesh repair.
3. Recurrence is higher in cases of ventral hernia operated by onlay mesh repair.
4. Recurrence is higher in cases with co-morbidities such as obesity, diabetes, and multiparity.
5. Although time taken for surgery in onlay mesh repair is significantly less compared to pre-peritoneal mesh repair, complications associated with it limits its wider usage. Considering the burden of surgeries especially in third world countries with a limited number of surgeons, it could provide valuable alternative over the pre-peritoneal repair.
6. The ease of the procedure in performing onlay mesh repair over pre-peritoneal repair gives it the points over pre-peritoneal but associated complications limits its use.
7. Finally to conclude, "Pre-peritoneal mesh repair is superior to onlay mesh repair."

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**Table 16: Mean hospital stay**

Mean hospital stays in days (%)	de Vries Reilingh <i>et al.</i> <sup>24</sup>	Gleysteen <sup>23</sup>	Present series
Onlay	8.2	7.9	7.53
Pre-peritoneal	6.1	5.9	5.96

**Table 17: Recurrence**

Recurrence rate (%)	Gleysteen <sup>23</sup>	de Vries Reilingh <i>et al.</i> <sup>24</sup>	Present study
Onlay	20	23	13.33
Pre-peritoneal	4	0	0

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# Quality of Life and Psychiatric Co-Morbidity in Patient with Vitiligo

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## Abstract

**Background:** Vitiligo is an acquired discoloration of skin and has great cosmetic importance affecting 1-4% of the world's population. Men, women, and children with vitiligo face severe psychological disturbance and most of the time undiagnosed. Hence, the problem persists affecting mostly the individual's quality of life (QOL).

**Aim:** Assessing the QOL, and co-morbid depression in patients with vitiligo.

**Materials and Methods:** The study conducted at Private Nursing Home, Gulbarga, Karnataka. The patients registered for dermatologist consultation were also registered for consultation with psychiatrist to rule out major depression after detailed evaluation using standardized scales.

**Results:** Patients who had vitiligo had major depression, and their QOL was disturbed.

**Conclusion:** The finding provides the role of the psychiatrist in the field of dermatology to treat co-morbid major depression and improve QOL.

**Key words:** Depression, Quality of life, Vitiligo

## INTRODUCTION

Vitiligo a cosmetic problem, affects individuals emotional and psychosocial well-being.<sup>1,2</sup> Vitiligo has severe psychosocial and occupational problems. The emotional factors are associated in one-third of patients with skin conditions.<sup>3</sup> Several patients with vitiligo report low self-esteem and embarrassment leading to social isolation and emotional stress, particularly if the disease develops on exposed areas of the body. The stigma of the disease may affect a person's interpersonal and social behavior, which in turn increases the risk of major depression and other psychosocial disorders.<sup>4-7</sup> The overall mental health in vitiligo patients is poor<sup>8</sup> and leads to a dramatic decrease in quality of life (QOL).<sup>9</sup> The majority of vitiligo

patients experiences depression, anxiety, frustration, and embarrassment during social interaction and disturbances noted in interpersonal relations or beginning a new social or sexual relationship. Counseling and medications can help improve body image, self-esteem, and QOL of patients with vitiligo.<sup>10</sup>

## MATERIALS AND METHODS

A cross-sectional study conducted in the private nursing home, Gulbarga, Karnataka. Clinically, diagnosed vitiligo patients in the age group of 18-40 willing to take part in the study were included. Patients with personal and familial mental illness, substance abuse, and primary depression were excluded. The control group included age and sex-matched individuals. They had minor skin changes like acne, wrinkles, tanning.

Materials used were vitiligo area severity index, dermatology life quality index questionnaire (DLQI), montgomery-Asperger depression rating scale, Hamilton anxiety rating scale.

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## RESULTS

The sample consisted of 25.5% ( $n = 12$ ) males; females accounted for 74.4% ( $n = 35$ ). Among the subjects employed were 36.1% ( $n = 17$ ) unemployed were 76.5% ( $n = 30$ ). The patients who had the lesion on exposed area were 85.1% ( $n = 40$ ) and non-exposed area 14.8( $n = 7$ ).

Psychiatric co-morbidity consisted of 80.8% ( $n = 38$ ) out of which major depressive disorder accounted for 63.8% ( $n = 30$ ). The patient also had Social phobia with the highest prevalence at 82.9% ( $n = 39$ ). Some of them also had both major depressive disorder and social phobia and consisted of 57.4% ( $n = 27$ ). Suicidality was also seen in 31.9% ( $n = 15$ ) of patients, high risk intentionality in 8.5% ( $n = 4$ ), and low risk intentionality in 23.8% ( $n = 11$ ).

In present study 30 of 47 patients had major depressive disorder. Chi-square test on this data shows that exposed vitiligo and major depressive disorder are significantly related ( $P < 0.05$ ) (Tables 1 and 2).

A 39 of total patients had social phobia and all the patients with social phobia had vitiligo in exposed area. Chi-square test on this data shows that vitiligo in exposed area and social phobias are significantly related (Significant  $P < 0.05$ ).

In this study, 95% of the patients had elevated DLQI with very severe, moderate, and mild effect in 38%, 38%, and 19% of patients, The DLQI score ranged from 1 to

20 with mean DLQI score of  $8.86 \pm 4.26$  in patient and  $1.02 \pm 1.12$  in control group ( $P < 0.001$ ).

## DISCUSSION

Vitiligo lowers individual's QOL by affecting social relations, work, games and overall social life due to disfigurement.<sup>11</sup> The psychological impact can have serious implications in individual with dark skin, due to noticeable contrast.<sup>12</sup>

In this study, 95% of patient had elevated DLQI against 30% in control group. 76% of patients had high DLQI scores falling into severe (38%) and moderate effect group (38%), whereas not a single control had severe or moderate DLQI score indicating considerable effect of vitiligo on QOL of patient ( $P < 0.001$ ).

In our study, 63.8% of patients had major depression, which was similar to some other studies stating major depression in 69% and 46.2% cases.<sup>13,14</sup>

## CONCLUSION

The present study showed deterioration in QOL and higher prevalence of major depression in patients with vitiligo. 64% of patients suffered from major depression, which is not a coincident. The chronic progression of the disease, long-term treatment, lack of effective therapy, and unpredictable prognosis and therapy causes psychological distress, contributing to compromised QOL, as well as major depression in some patients. There is a significant role of mental health professionals to treat underlying depression and further improving the QOL of the individual.

**Table 1: Chi-square test to compare the proportions**

Socio-Demographic variable	n (%)		$\chi^2$ value	P value
	Vitiligo	Control		
Sex				
Male	12 (25.5)	13 (27.6)	0.00	1.000
Female	35 (74.4)	34 (72.3)		
Total	47 (100.0)	47 (100.0)		
Lesion				
Exposed	40 (85.1)	-	0.00	1.000
Non-exposed	7 (14.8)	-		
Total	47 (100.0)			
Occupation				
Employed	17 (36.1)	42 (89.3)	0.00	1.000
Non-employed	30 (76.5)	5 (0.6)		
Total	47 (100.0)	47 (100.0)		

**Table 2: Prevalence of depression in subject group based on MADRS scale**

MADRS classification	Frequency	Prevalence (%)
No-depression	30	63.8
Depression	17	36.1
Total	47	100.0

MADRS: Montgomery-asperger depression rating scale

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# A Study of Certain Femoral Metrics in South Indian Population and its Clinical Importance

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## Abstract

**Background:** An osteological study of femur provides useful data to understand various diseases of femur and serves as a guide for the treatment of various pathological conditions of it.

**Aim:** The purpose of this study is to determine the various parameters of femur among south Indian population and to compare them with the data available worldwide.

**Materials and Methods:** A total of 158 adult femora were used to measure femoral total length, femoral anterior neck length and femoral neck shaft angle at Government Mohan Kumaramangalam Medical College, Salem and Government Stanley Medical College, Chennai.

**Results:** The length of the femur range from 35.5 cm to 50 cm with mean of 41.66 cm. The anterior neck length range from 2 cm to 4cm with mean of 3.09 cm. The neck shaft angle range from 120° to 145° with mean of 134.15°.

**Conclusion:** The present study hence provides valuable parameters which would help the forensic anthropologists, orthopedicians, and prosthetics to deliver excellent performance in their respective specialties.

**Key words:** Anterior neck length, Femoral length, Femur, Neck shaft angle, Parameters

## INTRODUCTION

The femur is the largest and strongest bone in the body and the structure of its proximal portion allows the leg to move in three dimensions relative to the torso, thus serving as a linchpin of human mobility. Moreover, age related and pediatric disorders at this skeletal site are common and confer strong risk factors for current and future disability. In Orthopedic practice, operations on femur are the most common. Variations in hip morphology are also of critical interest to surgical planning where the ability to take hip morphology into account on a patient specific basis is crucial for success in choosing designs of implants and other structures used for hip replacements and augmentations of hip stability.<sup>1</sup>

Different authors have suggested that difference in parameters of bone exists among different races and have tried to figure out the relationship of these variations to increased development of hip osteoarthritis, femoral neck fracture and slipped capital femoral epiphysis.<sup>2-5</sup>

The purpose of this study is to determine the various parameters of femur among south Indian population and to compare them with the data available worldwide.

## MATERIALS AND METHODS

A total of 158 dry femora were collected randomly not knowing the sex and age of bone and studied at Government Mohan Kumaramangalam Medical College, Salem and Government Stanley Medical College, Chennai. Damaged, incomplete and unossified bones were excluded. All the bones intact and fully ossified belonging to the adult persons were collected for study. 158 femora were studied for following measurements:

1. The femoral length: With the help of osteometric board
2. The femoral anterior neck length: With the help of sliding caliper

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3. The femoral neck shaft angle: With the help of goniometer.

The femoral length is the total length of the bone measured with the osteometric board. Anterior length of neck is the distance between the base of head and intertrochanteric line at the junction of the front of neck with the shaft. The neck shaft angle is the angle made by the axis of the neck with the axis of the shaft. The axis of the neck and axis of the shaft were measured respectively as the line joining the two center points on the anterior surface of neck and the line joining the two center points on anterior surface of shaft.

## RESULTS

The results of the present study were the mean length of femur was 41.66 cm, left femur was 41.88 cm and right femur was 41.29 cm, the anterior neck length of the femur was 3.09 cm, left femur was 3.16 cm and right femur was 2.98 cm. The neck shaft angle of femur was 134.15°, left femur was 135.02°, and right femur was 132.66° (Table 1).

## DISCUSSION

### Femur Length

In our study, the average length of femur was 41.66 cm, right femur was 41.29 cm, and left femur was 41.88 cm. The femur length in different populations is tabulated (Table 2).

The difference in mean femoral length in between populations may possibly be a result of factors affecting bone morphology such as genetic constitution, diet, nutrition status, environment, and physical activity.

Our results are in agreement with Bhosale and Zambare.<sup>8</sup> In their study the mean length of left male femur was 45.23 cm that of left female was 42.04, the mean length of right male femur was 45.08 cm that of right female was 41.64 cm.

**Table 1: Results of femoral length, anterior neck length and neck shaft angle**

Parameters	Number	Mean	Range	SD
Femur length in cm				
Total	158	41.66	35.5-50	3.03
Left	100	41.88	36-48.5	2.82
Right	58	41.29	35.5-50	3.39
Anterior neck length in cms				
Total	158	3.09	2-4	0.49
Left	100	3.16	2-4	0.46
Right	58	2.98	2-4	0.53
Neck shaft angle in degree				
Total	158	134.15	120-145	5.52
Left	100	135.02	120-145	5.36
Right	58	132.66	123-145	5.56

SD: Standard deviation

Our values are similar to the study of Zuylan and Murshid<sup>6</sup> (in their study left femur length was 42.84 cm, right femur length was 41.68 cm).

### Anterior Neck Length

The neck of the femur in humans is a very important structural and functional specialization for man's erect posture.

The anterior neck length of femur in different populations is tabulated (Table 3).

The mean femur neck length in the present study was 3.09 cm, right femur neck length was 2.98 cm and left femur neck length was 3.16 cm, our values agree with Ravichandran *et al.* study,<sup>13</sup> in their study the mean femur neck length was 3.18 cm.

Our study is similar to that of de Sousa *et al.*,<sup>12</sup> in their study right femur neck length was 3.01 cm, left femur neck length was 3.05 cm.

**Table 2: Femur length in different population**

Authors	Population	Subdivision	Femur length in cm
Zuylan <i>et al.</i> <sup>6</sup>	Anatolian	Left	42.84
		Right	41.68
Pandya <i>et al.</i> <sup>7</sup>	Indian	Left	
		Male	45.33
		Female	42.04
		Right	
		Male	45.18
		Female	41.74
Bhosale and Zambare <sup>8</sup>	Indian	Left	
		Male	45.23
		Female	42.04
		Right	
		Male	45.08
		Female	41.64
Gujar <i>et al.</i> <sup>9</sup>	Indian	Left	43.65
		Right	43.99
Khan and Saheb <sup>10</sup>	South Indian	Left	44.58
		Right	44.66
This study (2015)	South Indian	Left	41.88
		Right	41.29

**Table 3: Anterior neck length of femur in different populations**

Authors	Population	Subdivision	Anterior neck length in cm
Siwach and Dahiya <sup>11</sup>	Indian		3.72
de Sousa <i>et al.</i> <sup>12</sup>	Brazil	Left	3.05
		Right	3.01
Ravichandran <i>et al.</i> <sup>13</sup>	Indian		3.18
Gujar <i>et al.</i> <sup>9</sup>	Indian	Left	3.42
		Right	3.45
Khan and Saheb <sup>10</sup>	South Indian	Left	3.64
		Right	3.61
This study (2015)	South Indian	Left	3.16
		Right	2.98

**Neck Shaft Angle**

The neck shaft angle varies with age, stature and width of pelvis. When this angle >135°, condition is known as coxavalga. When angle <120°, it is known as coxa vara. The angle of femoral neck is reduced with aging. In early infancy the neck shaft angle is about 150°, in childhood 140°, in adult about 125°, and in elderly about 120°.

The neck shaft angle was studied in different population and races such as Norwegian, Mexican, Brazilian, and Indian (Table 4).

The average neck shaft angle found in this study was 134.15° which was similar to the study of Khan and Saheb,<sup>10</sup> de Sousa *et al.*,<sup>12</sup> Huaglund and Low<sup>14</sup> and Gujar *et al.*<sup>9</sup> our values are higher than the study of Pujari *et al.*,<sup>18</sup> Isaac *et al.*<sup>17</sup> and Siwach and Dahiya<sup>11</sup> in Indian population.

These observations have profound implications. According to Siwach and Dahiya<sup>11</sup> and Noble *et al.*,<sup>19</sup> in case of total hip arthroplasty, it is mandatory that the design and dimensions of femoral components should match the anatomy of femur. Siwach and Dahiya had noted a geometrical discrepancy between western implants and our Indian femora.<sup>11</sup>

According to Reddy *et al.*, a strong correlation has been established between the occurrence of thigh pain and inadequate fit and fixation of the implant. It has been noted that there is an increase in the clinical outcome score, which was directly proportional to the degree of implant bone fit. In using implants which have been designed for our western counterparts, the chance of implant mismatch is much greater. This in turn may lead to increase in the rate of aseptic loosening, greater implant subsidence, and

increased incidence of anterior thigh pain, more number of intraoperative complications and shorter lifespan of the implant.<sup>20</sup>

The implant device and prosthesis designed for western skeleton are large in size, there angles, orientations and thread length also mismatch the femora. Implants that are designed by taking in to account anthropometric and bio mechanic data will help in designing patient specific implants thereby minimizing the complications.<sup>21</sup>

Numerous studies have also shown that there is increase in the rate of intraoperative complication in the event of using mismatched implants especially over size implants.<sup>22</sup>

From this study, it is evident that the regional variations in the parameters measured do exist when the data of two different countries are considered but within a country there is not much variation. The present study is to generate a database for femur to help in designing for future implant.

**CONCLUSION**

The results of the present study show that the Indian dimensions of the femur are different from the western standards. Therefore, this study will enlighten the biomechanical engineers to take a revolutionary step towards altering the implant designs to suit our Indian needs. The limitation of this study has been a small sample size hence a study with a larger sample size is warranted. Gender and age of the bones have not been taken into account in the present study warranting inclusion of these parameters in future.

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**Table 4: Neck shaft angle of femur in different populations**

Authors	Population	Subdivision	Neck shaft angle in degree
Hoaglund and Low <sup>14</sup>	England		136
		China	135
Reikerås <i>et al.</i> <sup>15</sup>	Norwegian		127.7
Garcia and Uribe <sup>16</sup>	Mexico		130
Isaac <i>et al.</i> <sup>17</sup>	South Indian		126.7
Siwach and Dahiya <sup>11</sup>	Indian		123.5
de Sousa <i>et al.</i> <sup>12</sup>	Brazil	Left	131.8
		Right	132.1
Ravichandran <i>et al.</i> <sup>13</sup>	Indian		126.55
Gujar <i>et al.</i> <sup>9</sup>	Indian	Left	136.6
		Right	136
Khan and Saheb <sup>10</sup>	South Indian	Left	136.9
		Right	137.3
Pujari <i>et al.</i> <sup>18</sup>	Indian		127.5
This study (2015)	South Indian	Left	135.02
		Right	132.66

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# A Case-Cohort Study on Clinical utility of Garenoxacin mesylate in Respiratory Tract Infections: A Retrospective Analyses

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## Abstract

**Background:** Clinical management of respiratory tract infections (RTI) in community settings remains a therapeutic challenge with the overbearing threat of antimicrobial resistance looming large, especially amongst Gram-positive organisms including *Streptococcus pneumoniae*. The new generation fluoroquinolones reflect a significant advance with clinical utility often delineated for patients with recurrent infections or with comorbid risk factors.

**Aim:** To assess the clinical role of fluoroquinolones or garenoxacin for RTI in community settings.

**Methods:** This retrospective case series study conducted during monsoon period comprised of patients receiving fluoroquinolones including garenoxacin for RTI. Patients were assessed subjectively for control of baseline symptoms. Therapeutic response was judged as a clinical success or failure signifying significant improvement or no significant improvement/persistence of symptoms respectively. Observed notable or serious adverse events (SAE) were collected for analyses.

**Results:** Retrospective analyses revealed 22 patients receiving garenoxacin as first-line empiric therapy amongst fluoroquinolone prescriptions for RTI. Significant comorbidities were associated in 64% cases. Garenoxacin therapy advised for 5 days in all cases established clinical success (100%) and failure (0%) with no reported cases of any SAE.

**Conclusion:** For management of RTI especially in settings of associated significant comorbidities fluoroquinolones remains empiric choice. Garenoxacin a novel des-fluoroquinolone presents clinical utility in RTI while offering high safety profile.

**Key words:** Fluoroquinolones, Garenoxacin, Levofloxacin, Moxifloxacin, Respiratory tract infection

## INTRODUCTION

Respiratory tract infections (RTI) are major global health problem in adult males and females. According to World Health Organization (WHO) report disease burden of RTI is estimated at 94,037,000 disabilities adjusted life years (DALYs) and 3.9 million deaths. While disease burden of lower RTI (LRTI) and upper RTI (URTI) is estimated at 90,748,000 DALYs and 1,815,000 DALYs, respectively.<sup>1</sup>

In India, according to WHO data LRTI accounted for 35.1/100,000 population deaths in 2008 and accounted for 20% of total mortality due to infectious diseases.<sup>2</sup>

Sinusitis is an important cause of URTI. Infectious Disease Society of America (IDSA) 2012 clinical practice guidelines for acute bacterial rhinosinusitis, recommends fluoroquinolones (levofloxacin, moxifloxacin) as an alternative for initial empirical antimicrobial therapy, while macrolides, 2<sup>nd</sup> and 3<sup>rd</sup> generation cephalosporin are no longer recommended.<sup>3</sup> European respiratory society and European society for clinical microbiology and infectious diseases recommends fluoroquinolones (levofloxacin, moxifloxacin) as alternate empirical therapy for community-acquired LRTI especially in setting of relevant bacterial resistance.<sup>4</sup> IDSA/American thoracic society consensus guidelines on management of

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community-acquired pneumonia in adults recommends fluoroquinolones as empirical treatment for outpatient treatment in presence of significant comorbidities, use of antimicrobials in previous 3 months or high-level macrolide resistance.<sup>5</sup>

Most common adverse effects associated with fluoroquinolones use are gastrointestinal (nausea, vomiting, diarrhea), central nervous system (CNS) (headache, dizziness), allergic (rash, pruritus). Less common but important adverse effects of fluoroquinolones include QTc prolongation, blood glucose alterations, hepatotoxicity, phototoxicity, peripheral neuropathy, and seizures.<sup>6</sup>

Garenoxacin a novel des-fluoroquinolone with modified structure activity relationship provides broad spectrum coverage against common respiratory Gram-positive, Gram-negative and atypical pathogens including *Streptococcus pneumoniae*, *Hemophilus influenza* and *Moraxella catarrhalis*. While offering lower minimum inhibitory concentration (MIC<sub>90</sub>) values, and higher area under the curve (AUC)/MIC<sub>90</sub> ratio against the majority of pathogens.<sup>7,8</sup> Efficacy and safety of garenoxacin has been well-documented in ≈20,000 patient database. Overall garenoxacin shows efficacy of 91-96% in RTI with highly established safety profile.<sup>7,9,10</sup>

The present study was conducted to evaluate retrospectively the clinical role of fluoroquinolones or garenoxacin in the management of RTIs while being prescribed as an empirical therapy in RTI.

## METHODS

A retrospective case series cohort was analyzed to evaluate the role of fluoroquinolones including garenoxacin as an empirical therapy for adults with RTI. Cases were identified from database of all adult patients who were treated for RTI between August and October 2014, where the provisional diagnosis was made by attending physician. Case of URTI and LRTI were identified as diagnosed by physician. Epidemiological, demographic, medical history, prior history of antibiotic or fluoroquinolone use, treatment, clinical outcome and adverse event data was gathered for analyses. Therapeutic response was judged as clinical success or failure signifying significant improvement or no significant improvement/persistence of symptoms respectively at the end of therapy. Serious adverse event (SAE) defined as hospitalization or prolonged hospitalization, disability, death, congenital anomaly, or medical abnormality of significance was confirmed to be reported to central or regional pharmacovigilance center by the doctor.

## Statistical Analyses

Descriptive statistics was used to tabulate the data with percentage rate calculated for all categorical nominal and ordinal data variables.

## RESULTS

During the monsoon season of August to October 2014, 48 cases of RTI treated with various fluoroquinolones involving Garenoxacin were identified. Amongst these 48 cases, all of the RTI cases treated with Garenoxacin mesylate ( $n = 22$ ) were further analyzed.

### Baseline Demographics

Out of 22 cases analyzed 82% were male and 18% were female (Table 1). Associated significant comorbidities were noted in 41% cases which included dyslipidemia, diabetes, and hypertension. Two cases had past history of treatment for tuberculosis. Associated concomitant risk factors were noted in 27% cases which included history of smoking and alcohol consumption. Concomitant medications included oral hypoglycemic, antihypertensive and hypolipidemic agents. None of the cases were prescribed antibiotics or fluoroquinolones other than garenoxacin. None of the cases had history of hospitalization or fluoroquinolone use in recent past.

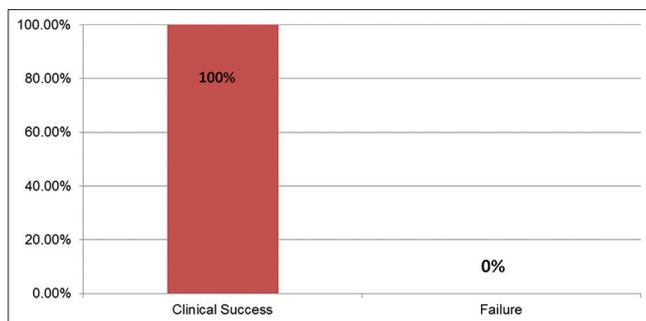
### Clinical Results

The cases included in the study presented with the complaints of fever (100%), cough (95%), expectoration (41%), breathlessness (23%), and dysphagia (5%). Garenoxacin was administered to these cases at a dose of 400 mg daily for 5-7 days. Complete resolution was noted in fever (91%), cough (100%), expectoration (100%), breathlessness (100%), and dysphagia (100%).

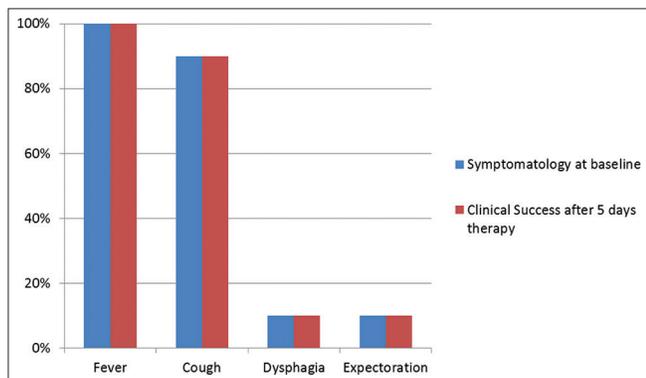
Therapy with garenoxacin was advised for 5 days in all cases. Clinical success was noted in all cases at the end of 5 days therapy. No case of therapy failure was reported (Figure 1). Detailed analyses of baseline symptomatology and clinical response after 5 days therapy in URTI and LRTI cases are detailed in Figures 2 and 3.

**Table 1: Baseline demographic parameters of the study**

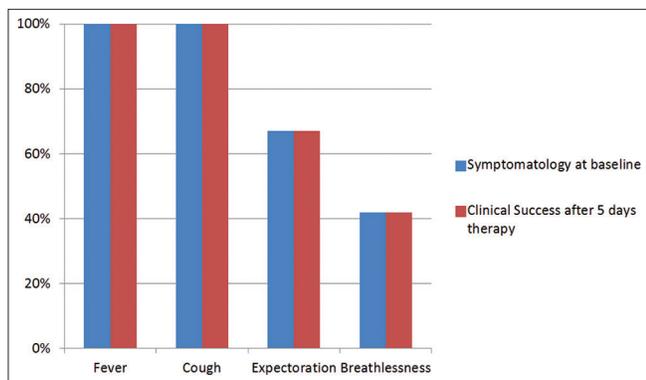
Total number of patients - 22	
Average age - 51.1 years	Average weight - 67.6 kg
Study details	Number of patients $n$ (%)
Gender	
Males	18 (82)
Females	4 (18)
Medical history	
Dyslipidemia	2 (9)
Diabetes	3 (14)
Hypertension	4 (18)



**Figure 1: Clinical Response at end of 5 days of therapy**



**Figure 2: Symptomatic response in upper respiratory tract infections cases (n = 10) at end of 5 days therapy**



**Figure 3: Symptomatic response in lower respiratory tract infections cases (n = 12) at end of 5 days therapy**

**Safety Profile**

None of the cases reported any adverse event or SAE, which required discontinuation of therapy or hospitalization.

**DISCUSSION**

RTIs are global health problem leading to significant morbidity and mortality. RTIs accounts for 6.4% of total global disease burden in terms of DALYs.<sup>1</sup> Fluoroquinolones (levofloxacin, moxifloxacin) use amongst frontline agents for empirical therapy of URTI and LRTI in community settings is well documented in

literature and also advised by leading respiratory disease treatment international guidelines. Empirical therapy of RTI in community settings with fluoroquinolones is especially advised in settings of associated significant comorbidities, high-level relevant bacterial resistance and use of antimicrobials in previous 3 months.<sup>3-5</sup>

Garenoxacin a novel des-fluoroquinolone lacks fluorine atom at C6 position unlike other fluoroquinolones with additional methyl isoindolyl and difluoromethoxy substitutions at C7 and C8 position respectively. Garenoxacin offers wide spectrum coverage against Gram-positive, Gram-negative and atypical pathogens including common respiratory pathogens like *S. pneumoniae*, Hemophilus influenza and Moraxella catarrhalis; while offering lower MIC<sub>90</sub> values, and higher AUC/MIC<sub>90</sub> ratio against majority of pathogens, that has important bearing for clinical efficacy while preventing resistance amongst Gram-positive pathogens including *S. pneumoniae*.<sup>7,8</sup> Garenoxacin shows efficacy of 91-96% in RTI over ≈20,000 patients database. Garenoxacin shows clinical efficacy of ≈94% in β-lactam resistant and macrolide resistant *S. pneumoniae*, most common pathogen responsible for RTI.<sup>7,9,10</sup>

In the presents study, associated significant comorbidities were present in 64% cases which included diabetes (14%), hypertension (18%), dyslipidemia (9%), smoking (23%), and alcohol (5%). In the present retrospective analyses garenoxacin demonstrates clinical success of 100% while being prescribed as empirical therapy for RTI in community settings.

Most common adverse effects associated with fluoroquinolones use are gastrointestinal, CNS, allergic while less common but important includes QTc prolongation, blood glucose alterations, hepatotoxicity, phototoxicity, peripheral neuropathy, seizures.<sup>6</sup> Recent years various fluoroquinolones were withdrawn from the U.S. market because of serious adverse drug effects includes gatifloxacin (dysglycemia), sparfloxacin (QTc prolongation, phototoxicity).<sup>11</sup>

Clinical safety of levofloxacin has been well established over large data from various clinical trials and postmarketing surveillance studies. Amongst these 7,537 phase 3 clinical trials patients database reported adverse reactions with levofloxacin includes gastrointestinal disorders nausea (7%), diarrhea (5%), vomiting (2%), constipation (3%), abdominal pain (2%), dyspepsia (2%); Nervous system disorders headache (6%), dizziness (3%), insomnia (4%); and others (>0.1 to <1) includes cardiac disorders (palpitation, ventricular tachycardia, ventricular arrhythmia); metabolism disorders (hyperglycemia, hypoglycemia).<sup>12</sup> QTc prolongation may result potentially life-threatening ventricular arrhythmia like torsade de pointes.<sup>11</sup> There is a

recent report of QTc prolongation with 16.7% incidence in patients on levofloxacin involving 2,176 patients.<sup>13</sup> Similarly, there are reports of significant dysglycemia with levofloxacin.<sup>14,15</sup> A retrospective cohort study reported levofloxacin ( $n = 457,994$ ), crude incidence rates for severe hyperglycemia 0.18 per 1000 cases, while amongst diabetic patients odds ratio hyperglycemia with levofloxacin compared to azithromycin was 1.8.<sup>13</sup> Furthermore, there are sporadic reports of serious CNS effects with levofloxacin like 2 case reports of seizures and 1 case report of catatonia.<sup>11</sup>

Clinical safety of moxifloxacin is also well established based in large clinical trials and postmarketing surveillance data. Amongst these 14,981 phase 2-4 clinical trials patients evaluated for moxifloxacin gastrointestinal disorders nausea (7%), diarrhea (6%), vomiting (2%), constipation (2%), abdominal pain (2%), dyspepsia (1%); nervous system disorders headache (4%), dizziness (3%), and insomnia (2%) have been reported.<sup>16</sup> Simultaneously, there have been several nested case-control studies have suggested cardiac adverse events including arrhythmia with moxifloxacin or metabolic dysfunction involving hyperglycemia/dysglycemia.<sup>17-20</sup> A nested case-control analyses from cohort of 605,127 patients identified risk of serious arrhythmia with moxifloxacin (RR = 3.30).<sup>19</sup> Amongst the new 3<sup>rd</sup> and 4<sup>th</sup> generation fluoroquinolones moxifloxacin carries greater risk of QT prolongation.<sup>11</sup> A population-based cohort study involving diabetic patients published reported moxifloxacin ( $n = 4,221$ ) absolute risk of hyperglycemia was 6.9 per 1000 persons respectively. Adjusted odds ratio for moxifloxacin compared with macrolides for hyperglycemia was 2.48.<sup>20</sup>

Clinical safety of garenoxacin is well established over  $\approx 20,000$  patients involving various clinical trials and postmarketing surveillance data. A postmarketing surveillance conducted in Japan involving 6,412 patients reported total adverse reactions (3.45%) with garenoxacin includes gastrointestinal disorders (0.87%) nausea (0.06%), diarrhea (0.48%), vomiting (0.05%), nervous system disorders (0.20%), cardiac disorders (0.20%), and Metabolism disorders (0.20%).<sup>9</sup> A prescription event monitoring study involving 12,498 patients from 400 centers reported total adverse events (1.27%) includes diarrhea (0.13%), CNS side effects (0.06%), nausea and/or vomiting (0.5%), rash (0.02%), abnormal liver function test (0.02%) and dysgeusia (0.01%).<sup>10</sup> With no reports of torsade de pointes over database.<sup>9,10</sup>

## CONCLUSION

Fluoroquinolones are suitable agents for empiric therapy of RTI in community settings. Garenoxacin, a structurally modified des-fluoroquinolone offers higher potency

against common respiratory Gram-positive, Gram-negative and atypical pathogens while offering lowest MIC<sub>90</sub> against most of pathogens and high AUC/MIC<sub>90</sub> ratio, an indicator of fluoroquinolone potency. High safety profile of garenoxacin is well-documented over database of  $\approx 20,000$  patients, offers differentiated safety profile amongst fourth generation fluoroquinolones for broader clinical use in real world settings.

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# A Simple Tool for the Improvement of Outcome in Medical Education Technology Workshops

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## Abstract

**Background:** The Medical Council of India (MCI) has specifically indicated that every medical college should have a medical education unit to train teachers in Medical Education Technology (MET). They have also made it mandatory for all faculty members of all medical colleges to have a certified training on MET. Courses of MET workshops which are currently operating have been meticulously prepared under the supervision of MCI. However, like other branches of medicine, MET is also progressing day-by-day and, therefore, the relevant faculties and participants alike should brainstorm themselves and also some of them, if not all should devote themselves to bring newer tools, newer principles and newer methodologies for advancement of MET. In this study, our humble venture has been to try a new and simple tool for improvement in MET performance by the participants.

**Materials and Methods:** The participants of specially arranged MET courses for this study purpose in MGM Medical College, Kishanganj were divided into two groups: Group A and Group B. The first group (Group A) received and answered a questionnaire before the commencement of the course but the second group (Group B) did not. Both the groups, that is, all the participants received the same questionnaire and answered them at the end of the workshop. The scores of the two groups of the final test (post-test) were compared and analyzed statistically.

**Results:** Results showed that the average marks obtained by participants in the final examination (post-test) were  $14.92 \pm 1.90$  in Group A (who received both pre-test and post-test) compared to  $12.08 \pm 2.0$  in Group B (who received only post-test). The *P*-value was estimated to be 0.000.

**Conclusion:** In this study, the results show that when a pre-test is applied before the commencement of the MET the post-test scoring is significantly improved compared to the group of participants who did not receive the pre-test. However, further studies are needed in a larger scale and in a more elaborate and sophisticated way to vindicate the findings of this study.

**Key words:** Continuing education, In-service training, Medical education, Medical teaching, Tools in teaching

## INTRODUCTION

In older days, the practicing physicians used to take “apprentices” to assist them in their practice and in return promised to teach them “the art and mystery of physique, surgery and pharmacy.” With the explosion of medical knowledge in the 20<sup>th</sup> century, this informal teaching gave way to formal syllabi based curricular development.

Until the mid - 20<sup>th</sup> century, it was thought that medical training conferred on doctors not only the art of healing but also the ability to teach medical students how to heal. With the free availability of every kind of information in the electronic age, new pedagogical philosophy of self-directed learning is redefining the teacher’s role. The teacher is no longer “The sage on the stage,” but “a guide by the side.”<sup>1</sup> Medical teachers need to embrace the new pedagogy so that their students will not just master current knowledge, but learn how to keep pace with new knowledge as it unfolds. Medical students must not only learn facts but learn professional behavior and procedural skills.

Famous scientist Edmund Teller wrote, “Confusion is no bad thing; it is the first step towards understanding.”<sup>2</sup>

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Newcomers to the field of medical education could be forgiven for being confused. Medical education is a busy, clamorous place, where a host of pedagogical practices, educational philosophies, and conceptual frameworks collide. It is a place where academic journals vie for attention, institutions, and professional bodies compete for political leverage, and the wheel of reformed and improvement revolves faster than an often independently of the cycle of evaluation and research; and it is a place of increasing accountability and regulation because of its those proximity to one of the prime sociopolitical concerns of government, that of the standard of teaching in medical colleges boiling down ultimately to the health of the country.<sup>3</sup> Within the confines of this academic and political preserve lies the discipline of medical education.<sup>4,5</sup>

The Medical Council of India (MCI) through its regulation for undergraduate medical education, 1997 has specifically indicated that every medical college has a medical education unit to train teachers in Medical Education Technology (MET). This has become even more important with changing curricula and newer trains in medical education. Subsequently, the MCI has made it mandatory that all faculty members in a medical college must have attended the MET certificate course and its workshop. However, in recent years with the enormous development of computer science and information technology, the MET workshops which have been meticulously prepared by the MCI and faculties of various regional authorities of medical education under MCI need to be revised and improved continuously to keep pace with the rapidly progressive realm of medical education. This is why passion and enthusiasm is expected of the medical teachers, particularly, the MET workshop faculties to keep brainstorming their minds and work on various ideas and projects so that newer and newer tools, techniques, and principles are evolved so as to improve progressively the outcomes of the MET workshops in different centers across the country and also outside.

This is, therefore, a simple tool designed by us to develop the new method in MET workshops.

## MATERIALS AND METHODS

Two groups (A, B) of medical teachers were selected from MGM Medical College, Kishanganj, Bihar, for the study. Each group comprised of 25 medical teachers. The selection process was on a random basis. A topic was chosen from the course of MET workshop. 20 questions were prepared (10 multiple choice questions and 10 objective

type questions). Each questions carrying one mark. The questions were made to cover the basic terminology and concepts of the topic. The questions were peer reviewed. The participants were made to know beforehand about the purpose and method of the study. A verbal and informal consent from the participants were also obtained, and they were found to be interested in participation of the study. The trainer, a trained medical educator, was same for both of the groups (A, B). The group A was given prior questionnaire made beforehand as a pre-test. At the end of the training of 2 h with power-point presentation and interactive session, the same questionnaire was given as post-test. In case of training of Group B, only the same post-test questionnaire was given at the end of the training of 2 h with power-point presentation and interactive session.

## RESULTS

The results of the participants' scorings of pre-test and post-test of Group A were analyzed by Student's *t*-test depicted in Tables 1 and 2 in the result section. The scorings of the post-tests of both the A and B Group were analyzed by independent unpaired *t*-test which is depicted in Table 3 in the results section. The graphic representation of the results are given as bar diagrams in Graph 1 and 2. The calculation was done by using IBM SPSS Statistics version 20.0.

## DISCUSSION

The average marks obtained by participants in the final examination were 14.92 in Group A (who received both pre-test and post-test) and 12.08 in Group B (who received only post-test) which are statistically significant as analyzed by independent unpaired *t*-test by using IBM SPSS Statistics version 20.0. It is found that analysis of pre-test and post-test scorings of Group A is also statistically significant.

Thus, our results show that when a pre-test is applied before the commencement of the MET workshop the post-test scoring is significantly improved. No such study was done in on MET workshops in India or anywhere as revealed by net search. However, this study can compared with a

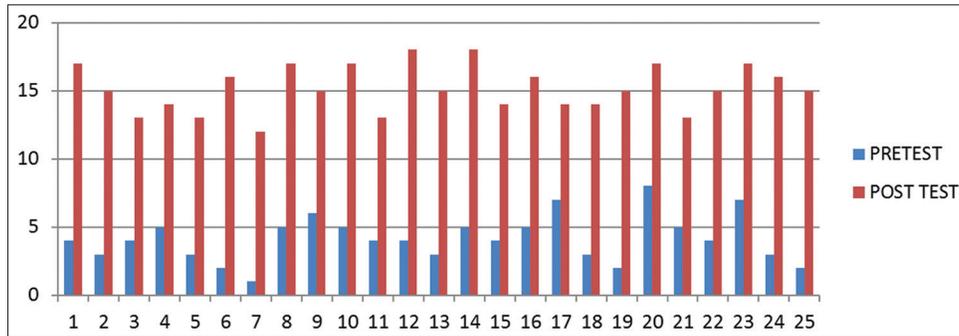
**Table 1: Descriptive statistics Group A: Mean, minimum, and maximum of scores obtained in pre-test and post-test**

Type of Test	<i>n</i>	Mean	Minimum	Maximum
Pre-test	25	4.1600	1.00	8.00
Post-test	25	14.9200	12.00	18.00

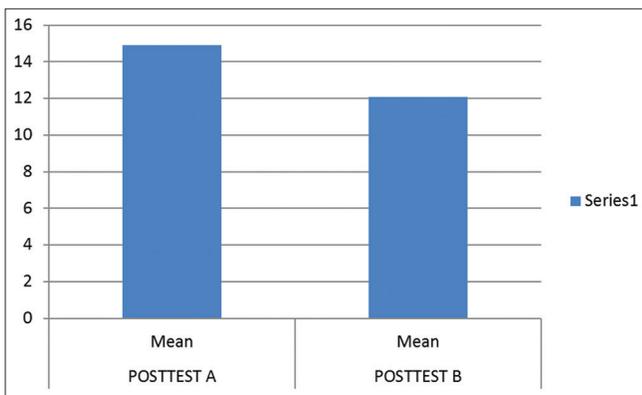
**Table 2: Comparison between post-tests between GroupA and GroupB**

Name of Groups	Paired differences					t	df	Significant (two-tailed)
	Mean	SD	SEM	95% CI of the difference				
				Lower	Upper			
Pair 1 VAR00001-VAR00002	-10.76000	1.94251	0.38850	-11.56183	-9.95817	-27.696	24	0.000

SD: Standard deviation, SEM: Standard of error mean, CI: Confidence interval



**Graph 1: Pre-test and post-test scorings of Group A**



**Graph 2: Post-test scorings of Group A and Group B**

similar study done on the beneficial effect of a pre-test on post-test in basic science lecture classes.<sup>6</sup>

Literature study reveals various tools and strategies which are described in detail in two kinds of literature.<sup>7,8</sup> Of course, teaching should always be maximally fruitful, as Doyle says “Teaching in the absence of learning is just talking.”<sup>9</sup> The literature on teaching is full of various ways that teachers can present contents and skills that will be enhanced the opportunity for the learners to learn.

It is equally filled with suggestions of what not to do in the teaching - learning session. However, there is no rulebook on which teaching methods match up the base to which skills, analytical tools and/or contents that are being taught. Students often have a little exercise in knowing, if the methods selected by an individual instructor was the best teaching methods or “Just a method” or simply the

method with which the teacher was most comfortable.<sup>10</sup> There are consistently high correlations between learners’ scorings in the course and overall ratings of the learners on the teachers and the course.<sup>11,12</sup>

Most universities while trying to understand the teachers’ efficacies embrace a process whereby students provide anonymous feedback at the end of each course they complete. These ratings of instructors’ effectiveness created a big hue and cry when they were first introduced,<sup>13</sup> and they create an enormous challenge for nearly every institution that uses them. Over the years, student evaluation has changed significantly especially in the areas of purpose and methodology. They have transformed from being primarily used to assist students to helping faculty members further developed and improve their teaching skills to assisting administrators with respect to various decisions.<sup>14</sup> Today students’ ratings are widely used for the purpose of making personnel recruitment and promotion decisions and faculty development recommendations.<sup>15</sup> The informations derived from these ratings help in making both summative and formative judgments.<sup>16,17</sup> Brascamp suggests that instructors use the data formatively to develop and improve their teaching skills. However, with our experience it can be inferred that each faculty and also participants should consciously and continually develop newer ideas and concepts and put them to challenges so that continuous inputs of newer methods of medical teaching evolve in a sustained manner. There is much debate within the higher education community on how teaching effectiveness may be defined.<sup>18</sup> For instance, Centra defines effective teaching

**Table 3: Caption: Comparison of post-test scores between Group A and Group B**

Type of Test	Mean	SD	Degree of freedom	Significance Test
Post-test A	14.92	1.9	48	0.000
Post-test B	12.08	2.0	48	0.000

SD: Standard deviation

as that “which produces beneficial or purposeful student learning through the use of appropriate procedure.”<sup>19</sup> It has been told that among the factors improving students’ attention and learning, apart from physical environment, bodily condition, students’ individual mood, length of lecture, and teacher’s personal appeal, one more important factor of immediate benefit is provision of a pre-test before the commencement of teaching session.<sup>20</sup> Our study has actually provided research evidence and hence reinforcement to this hypothesis.

## CONCLUSION

Our results show that when a pre-test is applied before the commencement of MET workshop the post-test scoring is significantly improved compared to the group of participants who did not receive the pre-test. However, further studies are needed on a larger scale and in a more elaborate and sophisticated way to vindicate the findings of our study.

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# Clinical Profile of Cardiac Failure and Its Correlation with Lab Markers and Outcome

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## Abstract

**Background:** Cardiac failure carries a high mortality and morbidity. Cardiac troponins and brain natriuretic peptide (BNP), are useful in the diagnosis and risk stratification of patients with heart failure (HF), are a better predictor of death. Both biomarkers are secreted directly, and almost exclusively by cardiac tissue and thought to be more sensitive than imaging or even invasive hemodynamics.

**Objectives:** The present study was done to assess the significance of troponin T and BNP levels in cardiac failure and their correlation with outcome.

**Materials and Methods:** The study included 196 patients with HF. Complete blood count, renal function test, liver function test, electrolytes, urine examination, electrocardiography, Chest X-ray, two-dimensional echo, cardiac troponin T, and serum BNP levels on admission were done for all patients. The study population was divided into 3 groups based on troponin T levels.

**Results:** 150 patients were in Group I with troponin T levels <0.03 ng/ml, 35 patients in Group II between 0.03 and 0.1 ng/ml, and Group III included 11 patients with levels more than 0.1 ng/ml. Mean duration of intensive care unit stay was 1.91 days in Group I, 4.03 in Group II, and 3.82 in Group III. Mean BNP values (957.3 in Group I, 2378 in Group II, and 3931.4 in Group III), systolic blood pressure (BP) (104 mm Hg in Group I, 96.4 in Group II, and 94 in Group III), and ejection fraction (41.92 in Group I, 34.18 in Group II, and 34.2 in Group III) were high in patients with higher troponin T values. All patients in group III required inotropic support and 45.5% patients had death.

**Conclusion:** An elevated cardiac troponin T values are associated with higher in-hospital mortality, lower ejection fraction and systolic BP, increased requirement of inotropes and prolonged intensive care.

**Key words:** Brain natriuretic peptide, Cardiac failure, Intensive care unit stay, Inotropic support, Troponin T

## INTRODUCTION

The incidence of heart failure (HF) is increasing because of improved survival after myocardial infarction. It is important to recognize that HF is a clinical syndrome arising from various causes. The American Heart Association and European Society of Cardiology have recognized the importance of simple and reproducible criteria and have developed guidelines for the diagnosis of

HF. According to these recommendations, the diagnosis is based on clinical parameters and other laboratory tests to determine the etiology and degree of functional impairment. As an example, the task force of The European Society of Cardiology for the diagnosis and treatment of acute congestive HF (CHF) recommended that a cardiac natriuretic hormone (brain natriuretic peptide [BNP]) assay should be included as a first step of in the diagnosis of HF along with electrocardiography (ECG) and chest X-rays. Missov *et al.*,<sup>1</sup> Missov and Mair<sup>2</sup> first reported the association between troponin and HF. Studies have indicated that elevated troponin concentrations in patients with HF are associated with more severe disease<sup>3,4</sup> and a worse prognosis.<sup>5-7</sup>

Reversible injury, from myocardial strain or subendocardial ischemia, could lead to transient changes in cell membrane

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permeability and leakage of cytosolic troponin. Troponin in cells is mostly bound to myofibrils suggesting the presence of more severe injury. Troponins are released in response to myocyte necrosis in patients with HF.<sup>8</sup> Cardiac troponins and BNP are secreted directly and almost exclusively by cardiac tissue. They indicate wall stress and injury which could be more sensitive than imaging or invasive hemodynamics. Both the biomarkers are clinically significant in view of the above features.

The need to counsel patients and select appropriate candidates for advanced therapies makes the proper assessment of HF prognosis very important. Prior small studies have suggested that routine measurement of cardiac troponins could help to identify HF patients in need of escalation of therapy. High troponin T is associated with adverse outcomes in chronic HF especially in patients with lower ejection fraction.<sup>9</sup> The role of troponin-T and BNP levels are being evaluated for population-based screening programs and prediction of prognosis in ambulatory CHF patients<sup>10,11</sup> and in chronic kidney disease for determining outcome and prognosis.

The present study was aimed at evaluating the significance of troponin-T levels in patients presenting with acute CHF in relation to diagnosis and assessment of prognosis. Also we wanted to study the correlation of troponin T with of left ventricle function, in-hospital mortality, BNP, duration of intensive care unit (ICU) stay, and systolic blood pressures (BP).

## MATERIALS AND METHODS

This was a cross-sectional study of 196 patients with HF admitted in Sri Ramachandra Medical College and Hospital from the year 2008 to 2010. All patients fulfilling inclusion criteria (acute cardiac failure as per Framingham criteria) were screened and investigations done. The patients with age <18 years, serum creatinine more than 2.0 mg/dl, sepsis, acute coronary syndrome, liver disease, and malignancy were excluded from the study. A detailed history was taken from all patients, and a thorough physical examination was done.

Framingham criteria were used for the admission diagnosis of all patients - diagnosis of CHF requires the simultaneous presence of at least two major criteria or one major criterion in conjunction with two minor criteria. Minor criteria are acceptable only if they cannot be attributed to another medical condition (such as pulmonary hypertension, chronic lung disease, cirrhosis, ascites, or nephrotic syndrome).

Complete blood count, renal function test, liver function test, electrolytes, urine examination, ECG, chest X-ray, and two-dimensional echo were done for all patients. Cardiac troponin T and serum BNP levels on admission were done. Cardiac troponin T was measured by the Roche cardiac T quantitative test which is an immunological test for the detection in venous blood for use with COBAS h 232 instrument. The study population was divided into three groups based on troponin T levels. Group I included 150 patients with troponin T levels <0.03 ng/ml, 35 patients in Group II with levels between 0.03 and 0.1 ng/ml, and Group III included 11 patients with levels more than 0.1 ng/ml.

The collected data was analyzed using the Statistical Package of Social Sciences (SPSS) software. Data were expressed as the mean  $\pm$  standard deviation. A  $P < 0.05$  was considered statistically significant.

## RESULTS

The study included 196 patients (168 males and 28 females). Eight patients were in the age group of 18-40 years, 69 patients between 41 and 60 years, and 119 patients above 60 years of age.

Out of 196 patients, 76.5% patients had troponin T levels <0.03, 17.9% patients had troponin T levels between 0.03 and 0.1, and 5.6% patients had troponin T levels >0.1, thus the majority of patients had low troponin T levels (Table 1).

Mean duration of ICU stay was 1.91 days in Group I, 4.03 in Group II, and 3.82 in Group III. Mean BNP values (957.3 in Group I, 2378 in Group II, and 3931.4 in Group III), systolic BP (104 mm Hg in Group I, 96.4 in Group II, and 94 in Group III), and ejection fraction (41.92 in Group I, 34.18 in Group II, and 34.2 in Group III) were high in patients with higher troponin T values. All patients in Group III required inotropic support and 45.5% patients had death. All were statistically significant except for systolic BP (Table 2).

## DISCUSSION

Troponin T values on admission correlate well with morbidity and mortality. Out of 196 patients, 76.5% patients

**Table 1: The study group**

Groups	Troponin T	Frequency	Percentage
I	<0.03	150	76.5
II	0.03-0.1	35	17.9
III	>0.1	11	5.6

**Table 2: Clinical and lab parameters with outcome**

Parameter	Group I	Group II	Group III	P value
Systolic BP - Mean value (mm Hg)	104	96.4	94	0.319
Inotropic support - Oral (N)	90	4	0	0.001
Inotropic support - Intravenous (N)	23	27	11	0.001
Ejection fraction - Mean value (%)	41.92	34.18	34.2	0.001
BNP mean value (pg/ml)	967.53	2378	3934.94	0.001
ICU stay (mean duration days)	1.91	4.03	3.82	0.001
Death (N)	2	7	5	0.001

BP: Blood pressure, BNP: Brain natriuretic peptide, ICU: Intensive care unit

had troponin T levels  $<0.03$ , 17.9% patients had troponin T levels between 0.03 and 0.1, and 5.6% patients had troponin T levels  $>0.1$ , thus the majority of patients had low troponin T levels. In a study by Peacock *et al.*,<sup>12</sup> Troponin was measured at the time of admission in 84,872 of 105,388 patients (80.5%) who were hospitalized for acute decompensated HF. Of these patients, 67,924 had a creatinine level of  $<2.0$  mg per deciliter. Cardiac troponin I was measured in 61,379 patients, and cardiac troponin T in 7880 patients (both proteins were measured in 1335 patients). Overall, 4240 patients (6.2%) were positive for troponin. Thus, the frequency correlated well with the present study.

The mean duration of ICU stay was lower (1.91 days) in patients with low troponin T value ( $<0.03$  ng/ml), and was highest (4.03 days), for the patient group whose troponin T were between 0.03 and 0.1 ng/ml. The mean duration for ICU care for patients with troponin T above 0.1 ng/ml was 3.82 days. The lower value of mean for the patient group with troponin T above 0.1 ng/ml was 3.82 days can be explained by the fact that early deaths in this subgroup resulted in shorter ICU stay compared to the patients group whose troponin T were between 0.03 and 0.1 ng/ml. In the study done by Peacock *et al.*, the median ICU stay was 4.1 for patients who were positive for troponin and 3.7 who were negative for troponin.

In the present study, patients with high troponin levels ( $>0.1$  ng/ml) had low mean systolic pressures of 94 mm Hg and patients with low troponin levels ( $<0.03$  ng/ml) had higher mean systolic pressures of 103.9 mm Hg. Thus, patients with higher troponin T values were associated with lower systolic pressures and the results correlated well with the above studies. In the study done by Peacock *et al.*, patients with high troponin had lower systolic BP on admission, than those who had normal troponin. In one small study by Koide *et al.*,<sup>13</sup> there was no significant differences of BP between the two groups. In another small study by Angheloiu *et al.*,<sup>14</sup> systolic BP correlated well with troponin levels.

We measured serum troponin T, plasma BNP, and left ventricular ejection fraction (LVEF) on admission. In the present study, the mean BNP for patients with troponin T values  $<0.01$  ng/ml was 967.53 and for the patients with troponin T values above 0.1 ng/ml was 3934.94. The mean BNP rise is proportional to an elevation of troponin T values. We hypothesize that an increase in troponin T concentrations is an expression of ongoing myocyte injury unmitigated by treatment of CHF and associated with a greater rise in BNP concentrations. Similar observations were in a study by Sato *et al.* In a small study by Koide *et al.*, patients in high troponin T group were significantly older and had a higher BNP on admission, as well as a higher prevalence of diabetes, and worse NYHA functional class at discharge. They also had higher discharge levels of BNP.

The measurement of troponin levels in patients who present with HF could provide independent prognostic information regarding in-hospital death and other clinical outcomes and can be useful for risk stratification of such patients. Ishii *et al.* reported a weak correlation between troponin T and BNP concentrations and suggested that markers specific for ongoing myocardial damage and left ventricular overload reflect different aspects of the pathophysiology of CHF and may identify different groups of patients at risk.

In the present study, the ejection fraction was highest (41.92) for patients with troponin  $<0.03$  ng/ml and lower (34.18) for patients with troponin T value more than 0.1 ng/ml, elevated levels were associated with decline in LVEF and higher mortality rates. Increased wall stress and myocyte death may explain the mechanisms. Increased wall stress may directly activate intracellular signaling cascades and decreased subendocardial perfusion even in the absence of coronary artery disease, resulting in a decline in systolic function. In the study done by Peacock *et al.*, patients with high troponin had lower ejection fraction on admission.

In the present study, 45.5% of patients died in the subgroup of patients with higher troponin T (more than 0.1 ng/ml) and 20% of died in subgroup of patients with troponin T (0.03-0.1 ng/ml), whereas only 3.1% deaths were observed in patients with low troponin T ( $<0.03$  ng/ml). Mortality was higher as the troponin T value increased. As per the available literature, persistently elevated levels were associated with a decline in LVEF and higher mortality rates. Additional factors, including activation of the renin-angiotensin system, sympathetic nervous system, and inflammatory cytokine system, have been implicated in provoking myocyte injury and cell death in HF.

The strength of the study is that we had observed a reasonable number to have a specific conclusion, but the

limitations remain. Our study differs from most of the prospective design by other studies and targeted focus on hospitalized patients. We did not do serial monitoring of troponin T and BNP levels and could not determine the persistence or variability of troponin T and BNP elevations during hospital stay. Furthermore, we could not do other available markers of cardiac failure.

## CONCLUSION

There is an association between elevated cardiac troponin levels and adverse events in hospitalized patients with acute decompensated HF. In patients with acute decompensated HF, an elevated cardiac troponin T values are associated with higher in-hospital mortality, lower ejection fraction and systolic BP, increased requirement of inotropes, and need for prolonged intensive care. The combination of measuring cardiac troponin levels, a marker for ongoing myocardial damage, and BNP, a marker for left ventricular overload, represents a highly effective means of risk stratification of patients with acute decompensated HF.

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# Acute Diarrhea and Acute Respiratory Infection among Less than 5 Year Old Children: A Cross-Sectional Study

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## Abstract

**Introduction:** Diarrhea and acute respiratory infections (ARI) are the major causes of morbidity and mortality in the developing nations. Diarrhea accounts for 9% of all the <5 year old children in 2012. The current estimates suggest that there are around 1.4 billion episodes of diarrhea per year with 9 million hospitalizations worldwide. ARI is responsible for about 30-50% of the visits to health facilities and about 20-40% of admissions to hospitals.

**Objectives:** (1) To estimate the prevalence of diarrhea and ARI among <5 year old children in a rural area. (2) To find out the association of certain demographic, socioeconomic, and environmental factors among <5 year of children with diarrhea and ARI.

**Methodology:** This cross-sectional study was done in Primary Health Centre, Nemam Tiruvallur district, Tamil Nadu. It included all the <5 years old children are residing in the area. The data was collected among 370 <5 year old children over a period of 3-month extending from November 2012 to January 2013 by simple random sampling.

**Results:** Among the selected 370 under 5 children, 51.1% were males, and 48.9% were females. The Prevalence of Diarrhea was 7.6%. The prevalence of ARI was 12.2%. The number of episodes for the past 1 year among <5 years old children was 1.64 episodes of diarrhea (standard deviation [SD] 1.1, median 2) and 2.58 episodes of ARI (median 2, SD 1.65).

**Conclusion:** The two major killers of children ARI and diarrhea are preventable by simple interventions like maintaining good personal hygiene and sanitation.

**Key words:** Diarrhea, Prevalence, Rural

## INTRODUCTION

The brunt of the health problems of our country is often felt by the vulnerable groups, i.e., mothers and children. Children under 5 years of age are the most affected by various common morbidities, some of which also lead to mortality in this vulnerable population. Around 10.6 million children in the world die every year before reaching their fifth birthday.<sup>1</sup> Diarrhea and acute respiratory infections

(ARI) are the major causes of morbidity and mortality in the developing nations. ARI is responsible for about 30-50% of the visits to health facilities and about 20-40% of admissions to hospitals.<sup>2</sup> More than 1.1 children under 5 years die from pneumonia every year, almost 17% of the under 5 deaths worldwide. In India, hospital records, from states with high infant mortality rate, show 13% of the inpatient deaths are due to ARI. Pneumonia was responsible for 18% of the under 5 deaths in India in 2014.<sup>3</sup> Diarrhea accounts for 9% of all the under 5 deaths in 2012.<sup>4</sup> Even though the overall diarrheal mortality has declined over the past few decades, the incidence of diarrhea has not changed much. The current estimates suggest that there are around 1.4 billion episodes of diarrhea per year with 9 million hospitalizations worldwide.<sup>5</sup> In India, diarrhea accounts for around 8% of deaths in <5 years old children's.<sup>6</sup>

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The top two major killers of <5 year old children is ARI and diarrhea which together accounts for 30% of all under 5 deaths, which amounts to 2.2 million deaths globally<sup>7</sup> by UN IGME in 2012. Although India has succeeded child mortality to considerable extent, considerable number of children are dying due to these two diseases due to piecemeal approach to service and provision and those at greatest risk are not being identified and reached<sup>8</sup> by UNICEF in 2013. This prompts the importance of taking up this study which will throw light on the prevalence of diarrhea and ARI among <5 year old children in the rural area of Tamil Nadu, India which will help to improve in the long run, the health status of children and the quality of life in rural India.

### Objectives

1. To estimate the prevalence of diarrhea and ARI among <5 year old children in a rural area
2. To find out the association of certain demographic, socioeconomic, and environmental factors among <5 year old children with diarrhea and ARI.

## METHODOLOGY

### Study Design

Population based cross-sectional study. Study area: This study was done at the Primary Health Centre area of Nemam belonging to Poonamallee block in the Tiruvallur district, Tamil Nadu, India. The Primary Health Centre, Nemam has 3 HSCs namely Nemam, Kuthambakkam, and Pappanchathram. Study population: It included all the <5 years old children's residing in the Nemam PHC area. It has a total of 2373 <5 year old children residing in the area, of which, 841 from Nemam Sub Centre, 541 children from Kuthambakkam, and 991 children from Pappanchathram. Study period: The data was collected over a period of 3-month extending from November 2012 to January 2012. Sample size: With available literature, the prevalence of diarrhea among <5 year old children according to National Family Health Survey 9% which was used to estimate the sample size. With the Limit of accuracy as 30% of anticipated prevalence and with Z (1- $\alpha$ /2) value of 1.96, the sample size calculated was 328. About 10% of sample size was added to take care of the refusal and non-participants. Hence, the total sample size arrived as 370. Sampling method: The sampling frame consisted of serially numbered children under 5 years of age listed out from the village wise family register of the each of the 3 sub-centers. Based on the population of <5 years old children's in each HSC, 131 children from Nemam HSC, 84 children from Kuthambakkam HSC, and 155 children from Pappanchathram HSC were selected using simple

random sampling method. The 370 random numbers were generated from the website [www.random.org](http://www.random.org)

## RESULTS

Among the selected under 5 children, 51.1% were males, and 48.9% were females. The mean age was 32.38 months (standard deviation [SD] 15.58) ranging from 1 to 60 months. Age group and sex distribution of the selected <5 years old children's is given in Table 1.

Among the selected 370 children, 70.8% of them were from nuclear family, followed by joint family 27.3% and 1.9% belonged to the extended nuclear family. The average family size was 1.87 ranging from 1 to 5. Their mean per capita income was Rs. 1373.5, with a median of Rs. 1250 (SD 806.4), with a range of Rs. 200-5000.

The mean birth weight of the <5 year old children was 2708.2 g (SD 514.7) ranging from a minimum of 1150-5000 g. The proportion of low birth weight was 14.3% (n53).

Among the 370 selected children, 3 of them had congenital anomalies. 1 child had Down's syndrome, and the other 2 had congenital heart defects. The immunization status was obtained for children aged 1-2 years ( $n = 113$ ). 82.3% of the children were fully immunized, and 17.7% children were partially immunized. Information about vitamin A supplementation was obtained for children more than 6 months of age ( $n = 359$ ). Among them, 80.5% had received vitamin A within the last 6 months, and the remaining 16.5% had not received any dose of vitamin A.

As per the criteria given by WHO,<sup>9</sup> a child was classified as at risk if any one of the 13 criteria were present. Among the selected 370 children, 207 (55.9%) were found to be at risk with a 95% CI of 53.32-58.48.

Personal hygiene was satisfactory among 59.2% of the caregivers and not satisfactory among the remaining 40.8% of the caregivers. Overcrowding was present in 42.4% of the houses, and the remaining 57.6% of the houses were not overcrowded. The sanitary latrine was

**Table 1: Age and sex distribution of under five children**

Age of the child (months)	n (%)		Number of children (n)
	Male	Female	
0-6	19 (48.7)	20 (51.3)	39
7-24	53 (62.4)	32 (37.6)	85
25-60	41 (48.8)	43 (51.2)	84
Total	189 (51.1)	181 (48.9)	370

**Table 2: Details of diarrhea and ARI**

Age of the child (months)	n (%)					
	Diarrhea			ARI		
	Male	Female	Total	Male	Female	Total
0-6	0 (0)	0 (0)	0 (0)	3 (100)	0 (0)	3 (21.4)
7-24	7 (58.3)	5 (41.7)	12 (10.9)	12 (66.7)	6 (33.3)	18 (16.4)
25-60	8 (47.1)	9 (52.9)	17 (6.9)	13 (54.2)	11 (45.8)	24 (9.8)
Total	15 (51.7)	14 (48.3)	29 (7.8)	28 (62.2)	17 (37.8)	45 (12.2)

ARI: Acute respiratory infections

present in only 26.8% of the houses and absent in the remaining 76.2%.

### Details of Diarrhea and ARI

Prevalence of diarrhea was estimated by asking the respondent about having episodes of loose stools within the last 2 weeks. Among the selected 370 children, 7.6% of them had diarrhea within the last 2 weeks (Table 2). Among those children, who had diarrhea, the majority of them (29.6%) were taken to the Nemam PHC for treatment, followed by home treatment (25.9%), 22.2% of them were taken to the Poonamalle District hospital, 14.9% were treated in private hospital, and the remaining 7.4% were treated in the HSC. The respondents were enquired about the number of episodes of diarrhea in the past 1 year, and it was found that 89.2% had <3 episodes of diarrhea. The details of the number of episodes of diarrhea are given in Table 3.

The prevalence of ARI was estimated by asking the caregiver of the child, whether the selected child had been ill with a cough accompanied by short, rapid breathing which was chest related in the last 2 weeks preceding the survey. The prevalence of ARI was 12.2% (Table 2). Among those children with ARI, the majority of the children 46.9% were taken to Nemam PHC for treatment, 25% of them were managed at home, 18.7% were taken to Poonamallee Hospital, 6.3% of them were treated in the HSC, and 3.1% were treated in private hospital. Details regarding the number of episodes of diarrhea and ARI in the past 1 year was collected, and it was found that the children had an average of 1.64 episodes of diarrhea (SD 1.1, median 2) and 2.58 episodes of ARI (median 2, SD 1.65); the details given in Table 3. Details about the association of diarrhea and ARI with the socioeconomic and environmental factors are given in Tables 4 and 5, respectively.

## DISCUSSION

The 2-weekly prevalence of diarrhea and ARI in this study was 7.6% and 12.2%, respectively. Similarly, the 2-weekly prevalence of diarrhea and ARI in under 5 children was

**Table 3: Details of number of episodes of diarrhea and ARI**

Number of episodes	n (%)	
	Diarrhea	ARI
<3	330 (89.2)	211 (57)
3-5	32 (8.6)	101 (27.3)
>5	8 (2.2)	58 (15.7)

ARI: Acute respiratory infections

**Table 4: Association of diarrhea and demographic, socioeconomic and environmental factors**

Particulars	Diarrhea		OR	95% CI	P value
	Yes	No			
Sex of the child					
Male	15	174	1.03	0.5-2.2	0.56
Female	14	167			
Modified Prasad's socioeconomic class*					
Class 3	3	9			
Class 4	7	72			
Class 5	28	342			
Immunization status of the child					
Partially immunized	2	18	1.04	0.2-5.2	0.62
Fully immunized	9	84			
Vitamin A supplementation					
Not given	2	49	0.42	0.09-1.8	0.19
Given	27	281			
Overcrowding					
Present	18	139	2.37	1.09-5.2	0.022
Absent	11	202			
Personal hygiene of the care giver					
Not satisfactory	17	134	2.19	1.01-4.7	0.034
Satisfactory	12	207			
Sanitary latrine					
Absent	24	245	1.88	0.7-5.1	0.12
Present	5	96			
At risk child					
Yes	15	192	0.83	0.4-1.8	0.63
No	14	149			

ARI: Acute respiratory infections, OR: Odds ratio, CI: Confidence interval, \* $\chi^2$  for linear trend is 7.92, df=2, P=0.019

found to be 11.9% and 15.5% in Chaturvedi *et al.*<sup>10</sup> Panwar and Nandan.<sup>11</sup> reported the 2-week prevalence of diarrhea and ARI as 13.6% and 24.1%, respectively. DLHS 4 and 3 reported the prevalence of diarrhea and ARI as 5.5% and 5.7% and as 5.5% and 8.9%, respectively.

**Table 5: Association of ARI and demographic, socioeconomic and environmental factors**

Particulars	ARI		OR	95% CI	P value
	Yes	No			
Sex of the child					
Male	28	161	1.68	0.9-3.2	0.075
Female	17	164			
Modified Prasad's socioeconomic class*					
Class 3	0	10			
Class 4	6	73			
Class 5	25	256			
Immunization status of the child					
Partially immunized	1	19	0.43	0.05-3.6	0.38
Fully immunized	10	83			
Congenital anomaly					
Present	2	2	7.5	1.03-54.7	0.02
Absent	43	323			
Vitamin A supplementation					
Not given	10	41	2.03	0.93-4.4	0.06
Given	33	275			
Overcrowding					
Present	26	131	2.02	1.08-3.8	0.02
Absent	19	194			
Personal hygiene of the care giver					
Not satisfactory	34	117	5.49	2.9-11.3	<0.01
Satisfactory	11	208			
Sanitary latrine					
Absent	32	239	0.185	0.08-0.4	0.43
Present	13	18			
At risk child					
Yes	33	174	2.4	1.2-4.8	0.012
No	12	152			

ARI: Acute respiratory infections, OR: Odds ratio, CI: Confidence interval, \* $\chi^2$  for linear trend is 1.076, df=2,  $P=0.58$

Diarrhea was more common in 7-24 month age group than in 0-6 months or more than 25 months age group, though not statistically significant ( $P > 0.05$ ). Similar observations made in Stanly *et al.*<sup>12</sup> The reason could be due to weaning and exposure of children to various environmental conditions as the child begins to crawl and walk. ARI was more common in the infant age group (0-6 months). Though not statistically significant, similar results were observed in Kumar *et al.*<sup>13</sup>

The present study shows <5 year old children suffer about 2.58 episodes of ARI and 1.64 episodes of diarrhea per child year. On an average, <5 year old children suffer about 5 episodes of ARI<sup>2</sup> and 3 episodes of diarrhea<sup>14</sup> per child per year. Walke *et al.*,<sup>15</sup> Awasthi and Pande<sup>16</sup> report 4.1 episodes, 1.67 episodes of ARI per child per year, respectively. Sutariya *et al.*<sup>17</sup> states children suffer from 3.42 episodes of diarrhea per child per year. These differences in the incidence rates may be due to the fact that some studies have been done only in a part of the year, regional differences, and different questions used to estimate ARI and diarrhea in the studies.

Prevalence of diarrhea was significantly increased in those children belonging to a lower socioeconomic status, those in overcrowded houses and whose care giver had unsatisfactory personal hygiene. About 88% of diarrheal deaths worldwide are attributable to unsafe water, inadequate sanitation, and poor hygiene (WHO/UNICEF 2004). Our study also confirms the same. A study by Yavatmal Khadse *et al.*<sup>18</sup> had also stated that hand washing with soap and water after defecation and before feeding had a protective value against diarrhea. There was significant association between lack of personal hygiene and occurrence of diarrhea in the study by Stanly *et al.*<sup>12</sup>

Prevalence of ARI was significantly increased in children who had not received vitamin A supplements, children with congenital anomaly, those in overcrowded houses, whose care givers had unsatisfactory personal hygiene and those children who were found to be 'at risk'. Vitamin A deficiency is known to be associated with an increase in mortality and morbidity due to respiratory and intestinal infections.<sup>19</sup> In a randomized trial in India,<sup>20</sup> vitamin A supplements had no significant effect on the percentage of time ill or number of respiratory infection episodes. Children who received vitamin A had a significantly increased mean duration of diarrheal episodes. In our study, though there is a significant association of reduction of ARI prevalence with vitamin A, there is no significant association in the reduction of diarrheal prevalence. Hence, there is a clear need to undertake a comprehensive trial with adequate sample size and a standardized methodology that could give clear, unbiased, and convincing evidence on the role of routine vitamin A supplementation. Overcrowding has a direct relationship with the prevalence of ARI. The present study found a significant association between ARI and overcrowding. Various studies such as by Bipin *et al.*,<sup>21</sup> Rahman and Rahman<sup>22</sup> Gupta *et al.*,<sup>23</sup> and Berman *et al.*<sup>24</sup> found a similar association.

## CONCLUSION

The two major killers of children ARI and diarrhea are preventable by simple interventions like maintaining good personal hygiene and sanitation.

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# Physiological Responses of Yogic Breathing Exercise in Young Females

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## Abstract

**Introduction:** In present day, scenario stressful lifestyle, irregular eating habits and lack of exercise have led to emergence of cardio-vascular and respiratory diseases which were less common in older days when people had less stress and were physically more active as compared to present days. We have tried to study the possible beneficial effects of breathing exercises so as to prevent cardio-vascular and respiratory morbidity in young females.

**Purpose:** In the modern era, the interest of yogic practice of asanas and breathing exercises has increased in the general population for health benefits. The objective of the present study is to evaluate the effects of breathing yogic exercises of yoga on respiratory and cardio-vascular parameters in young females.

**Materials and Methods:** A study was conducted in the department of physiology LLRM Medical College, Meerut. Case material for the study comprises of 30 female students of age group between 17 and 22 years. The selections of these students were done on a voluntary basis, and written consent from each one of them was taken. These students were divided into two groups, each comprising of 15 students. Group 1: This consists of 15 students who were kept as a control group. Group 2: This consists of another 15 students who practiced respiratory yogic exercises daily for 20 min, for 3 weeks.

**Result:** There was a significant reduction in resting pulse rate, and there is no significant change seen in peak expiratory flow rate and systolic blood pressure in group 2 after 3 weeks of yogic exercises.

**Conclusion:** The above study showed beneficial effects of regular breathing exercises on cardio-vascular functions in normal healthy individuals.

**Key words:** Blood pressure, Breathing exercises, Heart rate, Peak expiratory flow rate, Yoga

## INTRODUCTION

Stress and faulty life style are the major contributors to many diseases of modern civilization, such as obesity, hypertension, coronary artery disease, and diabetes mellitus.<sup>1,2</sup>

A carefully designed stress reduction program such as yoga has been shown to play a major role in recovery

and contribute to improved general health. It has gained immense popularity as a form of recreational activity all over the world. Its possible contributions to healthy living have been studied and many interesting scientifically based revelations have been made. Regular yogic practice results in a reduction in intrinsic neurohormonal activity such as a decrease in fasting blood glucose level. A few months practice of yoga (asana, pranayamas, meditation, or various combinations of these) triggers neurohormonal mechanisms that bring about health benefits.<sup>3</sup>

Yoga is a tradition of health and spirituality that evolved over a period of some 5000 years. The principles of yoga practice involve, the adoption and maintenance of psychophysical posture along with controlled breathing techniques it forms the basis of yoga's mind-body integration work.

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Psychological and social stressful stimuli affect hypothalamic-pituitary-adrenal axis due to which there is imbalance of equilibrium of various hormones, such as glucocorticoids and aldosterone, which increases blood volume causing increase in blood pressure and impose strain on heart.<sup>4</sup>

By giving rest to body and mind yoga maintains equilibrium and can prevent many disorders of psychosocial origin.<sup>5</sup>

The present study is done to see the response of short term (3 weeks) practices of yogic respiratory exercises on various cardiac and respiratory parameters.

## MATERIALS AND METHODS

This study was conducted in the department of physiology, LLRM Medical College, Meerut.

Case material for the study comprises of 30 female medical students of age group between 17 and 22 years. These selections of students was done on a voluntary basis, and written consent from each one of them was taken before the study was conducted (Figure 1).

Our subjects were divided into two groups, comprising of 15 students in each group.

Group 1: This consists of 15 students who were kept as a control group.

Group 2: This consists of another 15 students who practiced respiratory yogic exercises every day for 20 min and meditation for 10 min, for 3 consecutive weeks.

All subjects were under uniform dietary habits and received same yoga training for 3 weeks daily between 4 and 5 pm.

The different exercises practiced were: (a) Anulom - vilom, (b) kapal bhati, and (c) bhramari followed by 10 min meditation.

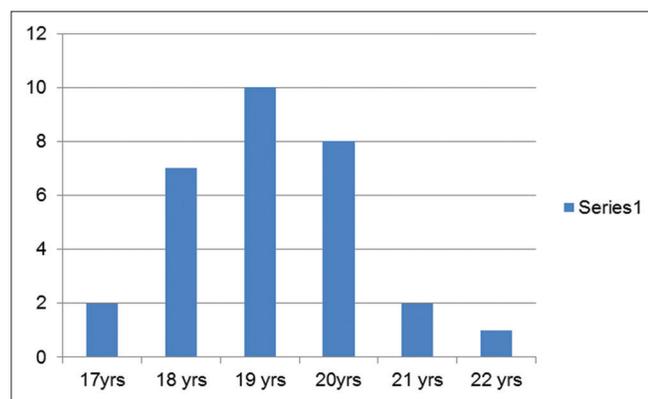


Figure 1: The age of subjects

Anulom vilom technique - Close right nostril with right thumb inhale slowly through left nostril remove right thumb from right nostril use ring and middle finger to close left nostril exhale slowly and completely inhale through right nostril with maximum inhalation close right nostril and open the left breath out slowly through left nostril continue for 15 min.

Kapalbhati technique - Inhale maximum air through the nostril and exhale through both nostrils forcefully repeat for 15 min take 1 min rest after every 5 min.

Bhastrika technique - Breath in deeply through nostrils and then breath out quickly through nostrils repeat the process, continue for 5 min.

Parameters studied were:

1. Systolic blood pressure (SBP) in mm Hg, measured by using mercury sphygmomanometer
2. Heart rate per minute, measured by palpatory method, in right radial artery
3. Peak expiratory flow rate (PEFR) recorded by wright's mini peak flow meter.

## RESULT

The result was calculated as mean standard deviation. Student *t*-test was used to find the significance of study  $P < 0.05$  was considered statistically significant.

### SBP

The mean SBP at the beginning of our study was  $125 \pm 7.8$  mm Hg, it reduced to  $120 \pm 7.4$  which apparently shows a decline in the values but the  $P$  value is more than 0.05 thus the change being insignificant.

### Heart Rate

Mean resting heart rate at the beginning of our study was  $96.10 \pm 7.6$ . It reduced to  $94.00 \pm 7.19$  at the end of our study with a  $P < 0.05$  thus the change being significant.

### PEFR

The mean PEFR at the beginning of our study was  $402.4 \pm 59.8$ . It increased to  $418 \pm 67.7$  at the end of our study with a  $P$  value of more than 0.05 thus the change

Table 1: Average parameters before and after pranayam

Parameters	Before exercise	After exercise	P value
SBP	$125 \pm 7.8$	$120 \pm 7.4$	$>0.05$
HR	$96.10 \pm 7.6$	$94.00 \pm 7.19$	$<0.05$
PEFR	$402.4 \pm 59.8$	$418 \pm 67.7$	$>0.05$

$P > 0.05$  - insignificant,  $P < 0.05$  - significant, SBP: Systolic blood pressure, HR: Heart rate, PEFR: Peak expiratory flow rate

being insignificant although there is a definite increase in the mean PEFR (Table 1).

## DISCUSSION

Prayanamas are effective in reducing heart rate immediately, but there is no significant change in PEFR and SBP. Respiratory exercises cause contractions of respiratory muscles and abdominal muscles.

The decrease in heart rate suggests an increase in parasympathetic activity.

Decrease in heart rate and blood pressure shifts towards parasympathetic activation reported by Joseph *et al.*<sup>1</sup> and Anand.<sup>2</sup>

The effect on autonomic nervous system is brought by yogic exercises by influencing limbic system and higher centers of central nervous system as reported by Sevamurthy *et al.*<sup>3</sup>

Long term and regular practice of these yogic exercises causes an increase in baroreceptors activity and decreases sympathetic tone of blood vessels thereby maintain blood pressure to normal levels. In patient of hypertension by Vijayalakshmi *et al.*<sup>4</sup> Bhargava *et al.*<sup>5</sup> reported better peripheral circulation and blood flow to tissue by Gopal *et al.*<sup>6</sup>

Raghuras *et al.*<sup>7</sup> have reported kapalbhati produces sympathetic stimulation.

In our study, there is no significant changes are seen in PEFR and SBP as time period taken for the study is short.

Prayanamas may increase frequency and duration of inhibitory impulses by activation of pulmonary stretch receptors, which bring about withdrawal of sympathetic tone in blood vessels of skeletal muscles, leading to widespread vasodilation, thus causes decrease in peripheral resistance and thus decreases blood pressure.<sup>8</sup>

Similar result observed in a study conducted by Madanmohan *et al.*<sup>9</sup>

While practicing prayanama one concentrate on the act of breathing which removes attention from worries and distresses him. This stress free state of mind evokes relaxed responses in which parasympathetic nerve activity overrides sympathetic activity.<sup>10</sup>

These might be a few possible reasons for the significant improvement in cardiac functions. Blood pressure and pulse rate related with cardio-vascular system in the controlled autonomic nervous system.

Prayanam increases cardiac output, decreases hepatic blood flow, and increases peripheral vessel blood flow.<sup>11</sup>

Nadishuddhi prayanam brings balance in autonomic nervous system.<sup>12</sup>

A practice of yoga bring decline in respiratory rate by increasing sympathetic activity<sup>13</sup> and PEFR improves due to increase in respiratory muscle activity.<sup>14</sup>

The effect can be explained on:

He following basis that increase power of respiratory muscles that is due to hypertrophy of muscles during prayanamas.<sup>13</sup>

Stimulation of pulmonary stretch receptors by inflation of lungs reflexly relaxes smooth muscles of larynx and tracheobronchial tree.<sup>12</sup>

Yogic breathing descent diaphragm and increases the vertical diameter of thoracic cavity.

Yoga with its calming effect on mind can reduce and release emotional stress thereby withdrawing bronchoconstrictor effect<sup>13</sup> Madanmohan *et al.*<sup>9</sup> have reported that yoga training of 6 weeks duration attenuates the sweating response to step test and produces a marked increase in respiratory pressures and endurance in 40 mm Hg test in both male and female subjects. In another study, they reported that 12 weeks of yoga practice results in a significant increase in maximum expiratory pressure, maximum inspiratory pressure, breath holding time after expiration, breath holding time after inspiration, and hand grip strength. Joshi<sup>13</sup> have also demonstrated that 6 weeks of pranayama breathing course resulted in improved ventilatory functions in the form of lowered respiratory rate, and increases in the forced vital capacity, forced expiratory volume at the end of first second, maximum voluntary ventilation, PEFR, and prolongation of breath holding time. Similar beneficial effects were observed by Makwana *et al.*<sup>14</sup> after 10 weeks of yoga practice. An increase in inspiratory and expiratory pressures suggests that yoga training improves the strength of expiratory and as well as inspiratory muscles. Respiratory muscles are like skeletal muscles. Yogic techniques involve isometric contraction which is known to increase skeletal muscle strength. Breath-holding time depends on initial lung volume. Greater lung volume decreases the frequency and amplitude of involuntary contractions of respiratory muscles, thereby lessening the discomfort of breath holding. During yoga practice, one consistently and consciously over-rides the stimuli to respiratory centers, thus acquiring control over the respiration. This, along

with improved cardio-respiratory performance, may explain the prolongation of breath holding time in yoga-trained subjects.

The technique of Kapalabhati pranayama involves short and strong forceful exhalations, and inhalation happens automatically. Very few references are available on the effect of Kapalabhati pranayama training on cardio-respiratory parameters in individuals. Our results are in agreement with that of Raghuraj *et al.*<sup>7</sup> who found that practicing fast pranayamas such as Kapalabhati for 6 weeks lead to decrease in sympathetic activity and is not in agreement with observations of few other studies. Madanmohan *et al.*<sup>9</sup> evaluated the short term effect of 3 weeks of Bhastrika pranayama practice on cardio-respiratory variables and reported an increase in sympathetic activity.

## CONCLUSION

The present study suggests that regular practice of yogic breathing exercises improves cardio-vascular and respiratory functions, but the time period in this study is short, and thus the results were not significant for all the parameters except heart rate.

These findings, suggests incorporation of yogic breathing exercises can enhance efficiency by improving lung function capacity, reducing the resting heart rate, and SBP.

It is thus concluded that these results and their explanations would justify the incorporation of yogic breathing exercises as a part of our lifestyle in the prevention of age-related cardio-vascular complications.

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# Morbidity and Mortality Patterns of Late Pre-terms and Their Short-term Neonatal Outcome from a Tertiary Care Hospital Puducherry

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## Abstract

**Background:** Late pre-term is defined as those babies born between 34 and 36 weeks and 6 days. This group of pre-terms is commonly associated with various complications soon after birth.

**Objectives:** To analyze the short-term neonatal morbidities associated with these late pre-terms and to look into the maternal risk factors involved.

**Materials and Methods:** This hospital-based prospective study was conducted at Sri Manakula Vinayagar Medical College and Hospital, Puducherry. All live late pre-term infants (34 0/7-36 6/7) born between June 2012 and July 2015 were enrolled in the study. Detailed history of the maternal complications during pregnancy, parity, mode of delivery, sex, gestational age, birth weight, and neonatal complications were all entered in the pre-designed proforma. The outcome of the babies was accessed by their morbidities, mortality, duration of hospital stay, and readmission following discharge. Descriptive statistics was used in the study.

**Results:** A total of 112 late pre-term were included in the study group. The male to female ratio was 1.54:1. The major proportion (71.4%) of these neonates was small for gestational age. Premature rupture of membranes, pregnancy-induced hypertension, anemia, and oligohydramnios are significant maternal risk factors identified. Respiratory distress was the major morbidity noted followed by sepsis, hyperbilirubinemia, and feeding difficulties. The duration of stay in the hospital was more than 7 days in the majority of them, but the rate of readmission was relatively less in our study. Three late pre-terms died during the study period.

**Conclusion:** The majority of the late pre-terms requires medical interventions in the neonatal intensive care setup and, therefore, has to be closely monitored and preferably planned for a safe discharge.

**Key words:** Hypoglycemia, Jaundice, Length of stay, Premature birth, Sepsis

## INTRODUCTION

Late pre-term babies (LPTB) are those delivered between 34 (0/7) and 36 (6/7) weeks of gestation.<sup>1</sup> 70% of all pre-term deliveries constitute these late pre-terms.<sup>2</sup> They are physiologically immature and metabolically

unstable and hence are at great risk of various medical complications after birth.<sup>3</sup> The common problems encountered by these infants include a higher rate of respiratory morbidities,<sup>4,6</sup> metabolic complications such as hypoglycemia, hypothermia, hyperbilirubinemia<sup>7,8</sup> feeding difficulties, increased risk of sepsis, and intraventricular hemorrhage.<sup>9,10</sup> Hence, there is an absolute increase in the number of these pre-terms admitted to the NICUs World Wide.

Understanding the morbidities of these infants helps the treating newborn healthcare providers to anticipate them, to treat accordingly to reduce their mortality.<sup>11</sup> Very few

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studies<sup>4,12-14</sup> have been conducted in the past to assess the morbidity and mortality in this group. Hence, the present study was undertaken to address to the short-term morbidities of these LPTB and their neonatal outcome.

## MATERIALS AND METHODS

This hospital-based prospective study was conducted at Sri Manakula Vinayagar Medical College and Hospital, Puducherry. All live late pre-term infants (34 0/7-36 6/7 weeks) admitted to our hospital between June 2012 and July 2015 were enrolled in the study. Those pre-term infants who had major congenital anomalies or suspected chromosomal disorder were excluded. Parental consent was taken, and the study was approved by Institutional Ethical Committee.

The following maternal details like age of mother, parity, complications during pregnancy, mode of delivery, if lower segment cesarean section (LSCS) the indications were noted. The infant details include gestational age, sex and birth weight, and the morbidities observed were noted. The gestational age of the child were assessed from last menstrual period date, 1<sup>st</sup> trimester ultrasonography (USG) if available and by modified Ballard score. The interventions done for the needed pre-terms such as continuous positive airway pressure (CPAP)/ventilation, surfactant therapy, and inotropic support, were also entered in the predesigned proforma. The following criteria were used for assessing the various morbidities observed.

### Birth Asphyxia

Complete cessation of breathing, inadequate, or gasping for breath with Apgar<4 at 1 min. The requirement of post resuscitation is assessed as per NRP 2010 guidelines.

### Hypoglycemia

Blood sugars of <40 mg/dl in capillary or venous blood sample. The blood sugars were monitored 8-12 h in sick late pre-term, intra uterine growth restriction (IUGR), infant of diabetic mother and large for gestation, birth weight >2SD) infants. Random blood sugar estimation done if clinically indicated.

### Hypothermia

New born core body temperature <36°C.

### Jaundice

Clinically, visible jaundice requiring phototherapy/exchange transfusion as per hour specific total serum bilirubin normogram by American Academy of Pediatrics chart. Bilirubin estimation done as per clinical requirement.

### Hyaline Membrane Disease (HMD)

Presence of tachypnea respiratory rate >60/min, Nasal flaring, grunting, or retraction of chest wall with need of O<sub>2</sub> for more than 2 h after birth and or CPAP/ventilation. Supportive radiological findings were also considered.

### Transient Tachypnea of Newborn (TTN)

The clinical and radiographic features noted during the 1<sup>st</sup> h of life, which shows complete resolution by 24-48 h.

### Apnea of Prematurity

Respiratory pause for more than 20 s or accompanied by bradycardia (heart rate <100 beats/min) or cyanosis.

### Pneumonia

As diagnosed by clinical examination and supported by X-ray chest findings.

### Hypocalcemia

Blood total serum calcium concentration of <7mg/dl.

### Sepsis

#### Probable sepsis

Positive septic screen (two of the five parameters namely, total leukocyte count <5000/mm<sup>3</sup> or 15,000/mm<sup>3</sup>, band to total neutrophil ratio of >0.2 absolute neutrophil count <1800/mm<sup>3</sup> or >7200/mm<sup>3</sup>, C reactive protein >0.5 mg/dl, platelets <1 lakh/mm<sup>3</sup>).

#### Proven sepsis

Isolation of pathogens from blood or cerebrospinal fluid (CSF) or urine.

### Intraventricular Hemorrhage

Hemorrhage identified by serial cranial USG.

### Feeding Difficulties

Delay in initiation and maintenance of adequate oral milk intake was considered as feeding difficulties in the absence of sepsis and respiratory distress.

The hospital outcome was assessed in the form of various morbidities, mortality, duration of hospital stay, and readmission following discharge. All the data were entered into a predesigned proforma and analyzed using Epi info version 3.5.4. Descriptive statistics was used in the study.

## RESULTS

Out of 120 cases, admitted during the study period, 112 met the inclusion criteria, among which 68 (60.7%) were male, and 44 (39.3%) were female. Male to female ratio was 1.54:1.95 cases (84.8%) were inborn babies, and 17 (15%) were outborn. Among 112 late pre-terms, 52 (46.4%) had

gestational age between 34 (0/7) and 34 (6/7) weeks, while 32 babies (28.5%) had gestational age between 35 (0/7) and 35 (6/7) weeks and 28 (25%) babies had gestational age between 36 (0/7) and 36 (6/7) weeks. Table 1 depicts the distribution of babies in different gestational age groups. In 28 (25.1%) neonates, the weight was appropriate for gestational age while the majority of them 80 (71.4%) were small for gestational age (SGA). On analyzing the birth weight 92 babies (82%) were born with the birth weight between 1.5 and 2.49 kg, 14 (12.5%) late pre-terms had birth weight above 2.5 kg while 6 (5.3%) neonates had birth weight below 1.5 kg.

46 (41%) babies were born to a primigravida, 38 (34%) babies were born to the second gravida mother and the remaining 28 (25%) babies were born to gravida 3 and above. The number of babies born vaginally was 48 (42.8%) while 63 (56.2) babies were delivered by LSCS and one baby was delivered via forceps extraction.

Maternal risk factors were present in 86 late pre-terms which constitute about 76% of cases. No maternal risk factors were identifiable in 13 (11.6%) of cases. Fetal factors like previous pre-term delivery and IUGR were noted in 11.5% of the cases. Among maternal risk factors pre-term premature rupture of membrane (PPROM) and pregnancy induced hypertension (PIH) has major contributed to 19.7% and 18.6% of cases, respectively. Oligohydramnios and anemia in the mother are the other significant risk factors identified. Maternal conditions such as antepartum hemorrhage, gestational diabetes, and eclampsia were noted in 4.6%, 5.8%, and 3.4% of cases, respectively. Table 2 elaborates the various maternal risk factors identified in our study group.

Among the 112 late pre-term 93 (83%) required NICU admission for some interventions, while 19 (17%) did not require NICU stay. Respiratory distress (51.7%) and sepsis (50%) constitute the major neonatal morbidities. Among the respiratory morbidities, 24 (41.3%) neonates had respiratory distress secondary to TTN. HMD and pneumonia were identified as important case of respiratory distress in 20.6% of cases each. Apnea of prematurity was noted in 10 (17.2%) of cases. Congenital heart disease was identified in 5 (4.5%) neonates 4 had acyanotic and one had cyanotic heart disease. 52 (46.4%) neonates had probable sepsis while 4 neonates had culture proven sepsis of which 2 had *Klebsiella* isolated from blood, 1 had Group B streptococcus sepsis, and the other one had *Escherichia coli* isolated from CSF culture. Among the metabolic problems, neonatal hyperbilirubinemia, hypoglycemia, hypocalcemia was noted in 40.1%, 17.8%, and 4.5% of the cases, respectively. Table 3 illustrates the various morbidities observed in our late pre-terms of the

**Table 1: Distribution of late pre-terms in different gestational age groups**

Gestational age weeks (days)	Number of late pre-terms (n=112)	Percentage
34-34 (6/7)	52	46.4
35-35 (6/7)	32	28.5
36-36 (6/7)	28	25

**Table 2: The various maternal risk factors associated with late pre-term births**

Maternal risk factors	Number of late pre-terms (n=86)	Percentage
PPROM	17	19.7
Pre-term LSCS	9	10.4
Anemia	12	13.9
PIH	16	18.6
Multiple births	3	3.4
APH	4	4.6
Gestational diabetes	5	5.8
BOH	4	4.6
Oligohydramnios	11	12.7
MSAF	2	2.3
Eclampsia	3	3.4

PPROM: Pre-term premature rupture of membranes, LSCS: Lower segment cesarean section, PIH: Pregnancy induced hypertension, BOH: Bad obstetric history, APH: Antepartum hemorrhage, MSAF: Meconium stained amniotic fluid

**Table 3: Distribution of various morbidities observed in late pre-terms**

Morbidities	Number of late pre-terms (n=112)	Percentage
Respiratory distress	58	51.7
Cardiovascular problems	5	4.5
Sepsis	56	50
Jaundice	45	40
Hypothermia	18	16
Hypoglycemia	20	17.8
Hypocalcemia	5	4.5
Feeding difficulties	34	30.3
IVH	1	0.9
Birth asphyxia	10	8.9
Anemia of prematurity	4	3.5
NNEC	5	4.4

IVH: Intraventricular hemorrhage, NNEC: Neonatal necrotizing enterocolitis

112 neonates 60 late pre-terms required oxygen which contributes to 53.5%. Mechanical ventilation was required in 4 babies, 3 for HMD, and the remaining one neonate was ventilated for severe sepsis. Non-invasive positive pressure ventilation was required in 16 (14.2%) late pre-terms. 45 (40.1%) neonates required phototherapy while 12 (10.7%) of them required inotropic support. Table 4 highlights the various interventions done for late pre-term.

Regarding the stay in the hospital 13 (11.6%) neonates required <3 days, 56 (50%) neonates required 4-7 days,

**Table 4: Various interventions required for late pre-term babies**

Interventions	Number of late pre-terms (n=112)	Percentage
Oxygen	60	53.5
NIPPV	16	14.2
Mechanical ventilation	4	3.5
Inotropic support	12	10.7
Surfactant	3	2.6
Phototherapy	45	40

NIPPV: Non-invasive positive pressure ventilation

and 39 (34.8%) neonates required 7-14 days of hospital stay, 4 required more than 14 days of stay in the hospital. Among 112 neonates, 109 were discharged after successful treatment while 3 late pre-term expired. Among the discharged neonates 4 had readmission to the hospital 2 for feeding difficulties, one for probable sepsis and one for jaundice which accounts for 3.5%.

## DISCUSSION

A total of 112 LPTB enrolled during the study period 60.7% were males and females constituted 39.3% which was similar to the observation made by other studies.<sup>11,15,16</sup> The majority of our late pre-terms were (71.4%) SGA which is in contrast to the other studies<sup>16,17</sup> where the population of SGA were much lower, the increase is probably due to higher incidence of maternal complications like PIH and Anemia detected in our study.

Maternal risk factors for pre-term delivery was noted in 86 (76%) of the babies in whom the major risk factors identified were PPRM, PIH, anemia, and oligohydramnios in the decreasing order. PPRM was also identified as an important maternal risk factor in other studies.<sup>16,17</sup> The percentage of babies born by LSCS was 56.2% which was high compared to other studies.<sup>15,16</sup>

On analyzing the various morbidities, respiratory distress was seen in 51.7% of late pre-term which was relatively high compared to other studies<sup>11,16,18</sup> probably due to increased incidence of TTN (41.3%) in our study secondary to the high rate of LSCS. The other respiratory morbidities include hyaline membrane disease and pneumonia in 20% of the babies each.

Late pre-term infants were more susceptible to develop sepsis compared to term infants.<sup>19</sup> In the present study, sepsis was identified as the second commonest morbidity (50%) which was significantly high compared to other studies.<sup>5,16</sup> In our study, the incidence of neonatal hyperbilirubinemia is 40% which is similar to the

observations made by the other studies;<sup>13,18</sup> however, Jaiswal *et al.*<sup>11</sup> reported much higher occurrence of jaundice in his study. The other metabolic problems noticed include hypoglycemia in 17% of late pre-terms similar observations was made by Leone *et al.*,<sup>18</sup> but in other studies<sup>5,11,16</sup> the incidence of hypoglycemia was much lower. The incidence of various other morbidities, such as hypothermia, feeding difficulties, and birth asphyxia, was comparable to the study done by Ezhilvannan *et al.*<sup>16</sup> but the incidence of intraventricular hemorrhage and neonatal necrotizing enterocolitis was much lower in our study.

Overall 83% of late pre-terms had at least one neonatal morbidity requiring medical interventions and NICU care which was slightly high compared to other studies.<sup>11,17,18</sup> In our present study, more than 43 (39%) neonates required hospital stay for more than 7 days which was similar to the study done by Ezhilvannan *et al.*<sup>16</sup> 4 neonates were readmitted in our study which is less when compared to other studies<sup>11,16</sup> probably because of our strict policy to maintain a safe discharge of these late pre-terms. Three deaths were noticed in our study period which accounts for 2.6% comparable to other studies.<sup>14,16</sup> Two died due to severe sepsis and one due to intraventricular hemorrhage.

The limitation of the study was first the small sample size and it secondly it highlights only on the short-term neonatal morbidities, so further studies are required to know the impact of these morbidities and the long-term neurodevelopmental outcome.

## CONCLUSION

PPROM and PIH are the most common maternal risk factors identified. Respiratory distress, sepsis, and neonatal hyperbilirubinemia are the significant morbidity noted in our study. The majority of the late pre-term required some medical intervention and NICU stay hence all these venerable group should be closely monitored and preferably planned for a safe discharge. Therefore every effort should be made to extend the pregnancy if there is no undue risk to the mother and the fetus, and urgent steps are required to prevent iatrogenic late pre-term births.

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# Incidence and Profile of Neonatal Musculoskeletal Birth Defects at a Tertiary Hospital in North East India

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## Abstract

**Background:** Musculoskeletal birth defects happen when bone and muscle tissue develops abnormally in the newborn during fetal development. The resulting deformities are a burden to the family and associated with substantial morbidity and mortality.

**Objective:** To determine the incidence and clinical profile of the musculoskeletal defects present at birth in the newborn.

**Materials and Methods:** This is a single-center, prospective, observational study in a tertiary care hospital between September 2010 and August 2015 in North East India. All newborn admitted to neonatal care unit were screened for musculoskeletal birth defects. Newborn with congenital defects of other systems was excluded. Clinical examination, skeletal survey and laboratory work up were performed, and data were analyzed.

**Results:** A total of 3120 newborns were admitted during the study period. The overall incidence of the musculoskeletal birth defect was 13.46 per 1000 live births. 42 patients with a total of 93 variants of musculoskeletal birth defects, 46 major, and 47 minor, were analyzed. Male and Female ratio was 1.1:1. Multiple defects were detected in 57.14% with 35.71% involvement of the lower limb. Among the 46 major variants of the musculoskeletal defect, the most common was congenital talipes equinovarus (15.22%). The commonest risk factor associated was neonatal jaundice 15 (35.71%), and only 2 cases (4.76%) were admitted for multiple musculoskeletal defects. Out of 42 cases, 54.76% needed orthopedic consultation. The average duration of hospital stay was 6 days. 4 cases (9.5%) expired following medical condition.

**Conclusion:** Neonatal musculoskeletal birth defect is under reported though the incidence is not low as our finding show 13.46 per 1000 live births. These may be presenting as multiple or isolated musculoskeletal defect at birth with minor or major variants and needs orthopedic consultation to treat early and prevent long-term disability.

**Key words:** Birth defect, Disability, Early detection, Musculoskeletal, Prevention

## INTRODUCTION

Globally, the congenital defects contribute to a large fraction of childhood morbidity and mortality. Birth defects can be defined as structural or functional anomalies, including metabolic disorders, which are present at the time of birth.<sup>1</sup> The musculoskeletal birth defects cause

long-term disability in the survivors as well as an economic burden to the families and society at large. There is poor information regarding the prevalence of musculoskeletal birth defects since many countries does not have national representative data. The causative mechanism of birth defect is heterogeneous, but genetic aberrations play a significant role.<sup>2</sup> The musculoskeletal birth defects may have a genetic, infectious, or environmental origin. Some deformities like multiple joint contractures may indicate an underlying serious neurologic malformation.

Antenatal screening and examination of newborn infants for musculoskeletal birth defects facilitates early detection, treatment, and care. Neonatal screening program should include musculoskeletal examination in addition to the

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existing system of screening. Early, referral to concern specialist and appropriate treatment of musculoskeletal birth defects can prevent disabilities and reduces permanent morbidities among the survivors. Considering the inadequacy of reporting system and lack of data regarding musculoskeletal birth defects, we take up this study to detect incidence and clinical profile in all the neonates admitted to our tertiary care institute.

## MATERIALS AND METHODS

The present study is the single-center, prospective, observational study done in a tertiary care institute. All the newborns with musculoskeletal birth defect who were admitted to neonatal care unit during September 2010-August 2015 were enrolled after approval from the Institutional Ethical Committee. A written patient consent form was maintained and explained the outcome measures. All the children 0-28 days of age were eligible for the study after they were diagnosed clinically with musculoskeletal birth defects. Congenital malformations involving other systems were excluded from the study. The overall incidence, socio-demographic data, the reason for hospitalization, and duration of hospital stay were analyzed in addition to the clinical examination profiles. The musculoskeletal birth defects were categorized according to the site involves, severity in terms of major or minor and whether isolated or multiple were also recorded. The defects that had referral services for further management were identified. Data regarding maternal age, antenatal screening done, and neonatal risk factors were also recorded. Laboratory investigation, skeletal survey, and recording images were done as indicated. Follow-up plan of the cases was not included in the study. All the data were calculated and analyzed.

## RESULTS

The total of 3120 newborns were admitted to neonatal care unit during the study period. 42 cases of musculoskeletal birth defects were selected for the study after fulfilling the inclusion criteria. The overall incidence of musculoskeletal birth defects was 13.46 per 1000 live births. 23 birth defects involving other major systems were excluded from the study. Among the study group, male were 22 (52.38%) and female were 20 (47.62%). Male to female ratio was 1.1:1. The highest number of admission belongs to age group below 24 h of life (52.38%). The majority of cases 30 (71.43%) belong to the lower middle socioeconomic class. 32 mothers were in the age group 25 to 35 years (76.19%). Antenatal sonography reports were recorded in 25 cases, and 2 cases were detected with moderate to severe oligohydramnios. Not a single mother had undergone

antenatal screening with serum biochemical markers. None of the cases had a family history of the similar defect, and there was no history of co-sanguineous marriage among the parents. 6 cases (14.29%) were born to Primigravida. Only 3 cases (7.14%) were born before 37 weeks of gestation. Out of 42 cases, isolated musculoskeletal birth defects were detected in 18 cases (42.86%), and multiple defects were noted in 24 cases (57.14%) Among the multiple musculoskeletal birth defects, one case was diagnosed as arthrogryposis multiplex congenita (distal type) which is shown in Figure 1. Four cases had Down's syndrome (9.5%). Figure 2 shows another case of multiple defects with the absence of right foot, the absence of 2<sup>th</sup>, 3<sup>rd</sup>, 4<sup>th</sup> distal, and middle phalanges with cutaneous syndactyly of 2<sup>nd</sup>, 3<sup>rd</sup> and 4<sup>th</sup> proximal phalanges of both hands. Among the 42 cases, a total of 93 (2.2 per patient) variants of musculoskeletal birth defects were analyzed. 35.71% had involvement of lower limb birth defect. Out of 93 variants of musculoskeletal birth defects, the major



Figure 1: A child of arthrogryposis multiplex congenita



Figure 2: A child with absence of right foot and absence of 2<sup>nd</sup>, 3<sup>rd</sup>, 4<sup>th</sup> distal and middle phalanges with cutaneous syndactyly of 2<sup>nd</sup>, 3<sup>rd</sup>, 4<sup>th</sup> proximal phalanges of both hands

defect was 46 (49.46%), and the minor defect is 47 (50.54%) cases. The most common major musculoskeletal defect was congenital talipes equinovarus, 7 cases (15.22%). (Table 1)

Out of total 42 cases of musculoskeletal defects, 23 cases (54.76%) needed consultation with an orthopedic surgeon for the correction of deformity. The commonest risk factor for admission to neonatal care unit was neonatal jaundice (35.71%). Only 2 cases (4.76%) were admitted for multiple musculoskeletal birth defects. Table 2 The average duration of hospital stay was 6 days ranging from 6 h to 22 days. Out of 42 cases included in the study, 4 patients had expired (9.5%) resulting from associated medical conditions.

## DISCUSSION

Musculoskeletal birth defects remain public health burden because most of them remain hidden. The congenital malformations are seen in 3% of all newborn.<sup>3</sup> The musculoskeletal defect is one of the common congenital malformations present at birth in a newborn. In the present study, the incidence of musculoskeletal birth defect is 13.46 per 1000 live birth. In India, the prevalence of birth defect is 64.3 per 1000 live birth according to the data given in Birth Defects prevalence estimates in the South- East Asia region, 2006.<sup>4</sup> Nationally representative data on overall prevalence of musculoskeletal birth defect needs to be studied as it contributes to significant proportion of neonatal and child morbidity and mortality. In most of the studies for birth defects in India, the predominant

system involved was musculoskeletal system. In a study done by Muranjan and Vijayalakshmi, musculoskeletal birth defects among older children (0.08-11 years.) was found to be 16.3% which is quite high in comparison to the present study.<sup>5</sup> Suresh *et al.* studies show that with an estimated 25 million births every year, the absolute number of children born with birth defect in India would be in excess of 500,000.<sup>6</sup> In our study of 42 musculoskeletal birth defects, male children were more affected than female with male and female ratio of 1.1:1. The majority of cases (71.43%) belong to the lower middle-income group. In a study, about 94% of serious birth defects occur in middle and lower income countries.<sup>1</sup>

Antenatal diagnosis of birth defects is possible with antenatal sonography and biochemical screening. The facilities for both the diagnostic procedure are costly and not universally available. The same clinical sign or malformation may be cause by a variety of genetic defects in addition to the environmental causes. In the present study, none of the cases were detected by antenatal ultrasonography and biochemical enzyme studies were not done for all cases. Only 2 cases had oligohydramnios and one case with twin pregnancy. None of the mothers had a history of drug intake during the antenatal period. There was no similar musculoskeletal birth defect among the family members and siblings. Only 6 cases were first born child.

The present study also shows 24 cases of multiple musculoskeletal birth defects and 18 cases of isolated

**Table 1: Variants of musculoskeletal birth defects**

Major musculoskeletal birth defects	n=46 (%)	Minor musculoskeletal birth defects	n=47 (%)
Absence (2, 3, 4) distal and middle phalanges both hand	1 (2.17)	Bilateral anonychia of hand	1 (2.13)
Absent multiple ribs (left) 3 <sup>rd</sup> to 9 <sup>th</sup>	1 (2.17)	Bilateral hammer toe	3 (6.38)
Apodia (right lower limb)	1 (2.17)	Bilateral wide gaping of 1 <sup>st</sup> and 2 <sup>nd</sup> toe	9 (19.15)
Absent right thumb	1 (2.17)	Cleynodactyly	4 (8.51)
Cleft palate	3 (6.52)	Depress nasal bridge	10 (13.51)
Cleft lip	5 (10.87)	Low set ear	5 (10.63)
Congenital calcaneovalgus	1 (2.17)	Metatarsus adductus	4 (8.51)
CTEV	7 (15.22)	Overlapping of 1 <sup>st</sup> and 2 <sup>nd</sup> toe	2 (4.23)
Cutaneous syndactyly (2, 3) proximal phalanges of both feet	1 (2.17)	Rudimentary ear lobe (both)	2 (4.23)
Cutaneous syndactyly (2, 3, 4) proximal phalanges both hand	1 (2.17)	Short and broad finger of both hands	4 (8.51)
Flexion contracture of knee (both)	1 (2.17)	Sacral dimple	2 (4.23)
Flexion contracture of wrist (both)	2 (4.35)	Unilateral hammer toe 1	1 (2.13)
Genu recurvatum (both)	2 (4.35)		
Genu recurvatum (left)	1 (2.17)		
Hemi-vertebrae	2 (4.35)		
Hypermobility of the joint	6 (13.04)		
Imperforate (both) external auditory canal	1 (2.17)		
Macrocephaly	1 (2.17)		
Microcephaly	2 (4.35)		
Micrognathia	3 (6.52)		
Osseous polydactyly (L) thumb	1 (2.17)		
Osseous polydactyly (R) thumb	1 (2.17)		
Rudimentary left thumb	1 (2.17)		

CTEV: Congenital talipes equinovarus

**Table 2: Reason for indoor admission in neonatal care unit**

Condition	n=42 (%)
Multiple birth defect	2 (4.76)
Pre-term with low birth weight	3 (7.14)
Poor feeding with sepsis	6 (14.29)
Respiratory distress	6 (14.29)
Low Apgar score	10 (23.81)
Neonatal jaundice	15 (35.71)

musculoskeletal birth defect out of the total 42 cases. In a study done by Aase, the mechanism of isolated lesion is poorly understood but may include phenomena like somatic cell maturation, aberrant cell migration, deficient or excess cell division, and failure of cellular interactions.<sup>3</sup>

The combinations of birth defects appear to be random, but sometimes a specific pattern of defects can be recognized. Two cases of multiple musculoskeletal birth defects were also detected during our study period. One of the defects was distal arthrogryposis multiplex congenita. This could be due to environmental factors occurring in intrauterine life. The congenital contractures involving two or more body areas in extremities may be present as distal arthrogryposis. These congenital contractures tend to improve with age but do not completely disappear.<sup>7</sup> Another multiple defect was the absence of right foot (Apodia) with bilateral absence of middle and distal phalanges of 2<sup>nd</sup>, 3<sup>rd</sup> and 4<sup>th</sup> and cutaneous syndactyly of 2<sup>nd</sup>, 3<sup>rd</sup> and 4<sup>th</sup> proximal phalanges of both hands. In this case, only the limb defects were detected with no other systemic involvement. With proper prosthesis and other rehabilitation, baby may live a normal life. According to International Standard (ISO 8540 - 1: 1989) classification absence of foot including skeletal deficiency is a transverse tarsal and metatarsal total deficiency. It is a form of “congenital amputation” implying that a limb segment has been lost before birth which is partial failures of the formation.<sup>8</sup> The etiology could be genetic, teratogens, vascular disruptions, chemical, and radiation exposure.<sup>9</sup> In our study, the etiology of the defect could not be revealed.

From the present study, 93 variants of musculoskeletal birth defects were identified of which 46 (49.46%) major defects were detected and minor defects were 47 (50.54%). Out of total major variants, the most common defect was congenital talipes equinovarus, 7 cases (15.22%). Congenital talipes equinovarus is a deformity in which the foot is turned inwards to a varying degree. In the general population, the incidence of congenital talipes equinovarus (CTEV) is 1 in 1000 live births. There is a 1:800 chance of having this deformity; 1:3.5 chance in sibling and 1:3 chance in an identical twin.<sup>10</sup> In our study, the incidence

of CTEV was 2.2 per 1000 live birth admitted to neonatal care unit which shows a higher incidence in a high-risk group of neonates. There are inherited neonatal orthopedic conditions like CTEV present at birth, which may be underdiagnosed.<sup>11</sup> An equinovarus deformity present at birth should be brought to the notice of an orthopedic specialist at the earliest.<sup>12</sup> All our cases were referred to an orthopedic specialist for immediate management.

We also detected a case of mild Calcaneo-valgus deformity in one of the twins, whereas the another twin was normal in all the four limbs. Due to crowding of the uterine environment there is a greater risk of limb deformities in multiple pregnancies. During antenatal period, twin to twin transfusion syndrome may occur in monochorionic twins due to the arteriovenous anastomosis. One of the complications in the donor twin includes limb deformities.<sup>13</sup>

Of the total study patients, 23 (54.76%) cases were needed an orthopedic consultation for further management. Referral to the specialist concern is required for all the musculoskeletal birth defects to start timely treatment and achieve reasonable functionality. Treatment should be started as soon as possible after birth to prevent lifelong morbidity. During the first 3 weeks of life relaxin hormone remains in circulation that keeps the ligament relaxed and stretching treatment is successful.<sup>14</sup>

In a study done by Colvin and Bower, children with birth defects were also more likely to hospital admission for reasons other than birth defects.<sup>15</sup> In the present study, a neonatal risk factor which required hospital admission were calculated, and the most common risk factor was neonatal jaundice 15 cases (35.71%) followed by birth asphyxia 10 cases (23.81%). Only two cases of multiple musculoskeletal defects were admitted without any risk factor. This study indicates that one must not overlook the presence of musculoskeletal defect at the birth of a newborn.

Children with genetic diseases and chromosomal disorders had an average hospital stay of 7.1 days as compare to 3.5 days average stay for children without any pre-existing medical disorder.<sup>16</sup> In our study, the average duration of hospital stay was 6 days. Out of total 42 cases detected as musculoskeletal birth defects, 4 cases (9.5%) were expired. In developing countries like India, congenital malformations were the third commonest cause of perinatal mortality. According to National Neonatology Database, the primary cause of stillbirths and neonatal deaths (9.6%) is contributed by malformations.<sup>17</sup> This finding is near to our finding of neonatal deaths during the study period. WHO estimates that birth defects accounted for some 556,000 deaths worldwide and for 145,611 out of 1,564,530 neonatal deaths in the year 2012.<sup>18</sup>

Birth defects are an emergent health priority in developed countries. From the findings of the present study, it is evident that musculoskeletal birth defects are common. They account for 1.35% cases admitted to neonatal care unit (13.46 per 1000 live births). The limitation of the present study is that it being from a single resource limited center; the sample size is small, but the findings are quite remarkable. Birth defects remain under-recognized owing to poor information on prevalence, and many countries do not have nationally representable data. To detect the musculoskeletal birth defects, a careful clinical examination by the primary care pediatrician could be important. A complete physical examination should be performed to rule out co-existing musculoskeletal and neuromuscular problems.<sup>19</sup> The need for a thorough systematic physical examination at birth cannot be over emphasized. Non-operative treatment should be started as soon as possible following birth. Services and intervention for prevention, treatment, and care of children with musculoskeletal birth defects must be integrated into the existing health care services.

## CONCLUSION

The present study shows the incidence of musculoskeletal birth defects as 13.46 cases per 1000 live births admitted to our neonatal care unit indicating one of the common birth defects present in newborn. Multiple defects (57.14%) were more affected than isolated musculoskeletal birth defects. It is estimated that 49.46% of the cases were having major variants of musculoskeletal defects present at birth. Though the commonest reason for admission was neonatal jaundice, 54.76% of the cases required orthopedic consultation for the correction of deformity. Musculoskeletal birth defects are an emerging burden of tertiary care center and screenings of newborn infants for musculoskeletal birth defects by careful physical examination is needed. A multidisciplinary approach to identify, treatment and prevention of permanent disabilities are highly recommended. National data on musculoskeletal birth defects are under reported from resource-poor health care centers in India. Maintenance of musculoskeletal birth defects registries might play a vital role to understand the epidemiology and could be useful for policy makers to tackle the problem of birth defects. To conclude more studies on etiology, pathogenesis, early detection and

treatment of musculoskeletal birth defect is an important area of pediatric health care research.

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# C-Reactive Protein in Chronic Obstructive Pulmonary Disease, its Correlation with Lung Function and the Role of Statin in Chronic Obstructive Pulmonary Disease

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## Abstract

**Background:** The link between increased C-reactive protein (CRP) and the prediction of cardiovascular risk has suggested that there might be an association between chronic obstructive pulmonary disease (COPD) and the increased incidence of cardiovascular disease (CVD) among other comorbidities.

**Aim:** The present study was done to study the relationship between the biomarker of systemic inflammation viz. CRP and disease severity, functional status and outcome in COPD patients over a period of 120 days after an acute exacerbation.

**Materials and Methods:** An observational cross-sectional study was done on 179 patients with COPD presenting in acute exacerbation to Department of Medicine in Nehru Chikitsalay of B. R. D Medical College, Gorakhpur from January 2014 to June 2014. Forced expiratory volume, BODE index and COPD assessment test were studied. All patients underwent a detail history and clinical examination at presentation and on follow-up visits on days 15, 30, and 120.

**Results:** In present study out of 179 patients, 105 (58.65%) were male, and 74 (41.34%) were female. Most of the patients were in the age group of 50-70 years (60.88%). The CRP was raised ( $\geq 3$  mg/l) in 136 (75.97%) patients out of that 82 (79.61%) attended day 120 follow-up and the other, 43 (24.02%) patients did not have a raised CRP at the initial visit. Out of 27 patients who expired, 26 (96.29%) had raised CRP ( $\geq 3$  mg/l) at initial presentation. A total 28 patients were lost during follow-up.

**Conclusion:** We observed that not all COPD patients had a raised CRP but in those who had a raised CRP, its levels correlated with lung function and functional status of the individual and CRP trends could be a predictor of death. In our study, we found a definite correlation between CRP and lung function. COPD is the "cause or effect of systemic inflammation still needs to be established.

**Keys words:** C-reactive protein, Chronic obstructive pulmonary disease, Lung function

## INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a common, preventable lung disorder characterized by progressive, poorly reversible airflow limitation often with

systemic manifestations, in response to tobacco smoke and/or other harmful inhalational exposures.<sup>1</sup> Exacerbations and comorbidities contribute to the overall severity of disease and functional status in individual patients.<sup>1</sup>

COPD is frequently associated with comorbidities,<sup>1</sup> the most serious and prevalent being atherosclerosis cardiovascular disease,<sup>2</sup> anorexia,<sup>2,3</sup> lung cancer,<sup>1,4</sup> osteoporosis,<sup>3</sup> muscle weakness,<sup>1</sup> cachexia,<sup>3,1</sup> normocytic normochromic anemia, increased gastro esophageal reflux and clinical depression and anxiety. These comorbidities contribute to impaired functional capacity, worsening dyspnea, reduced health-related quality of life and increased mortality.

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There are several biomarkers of systemic inflammation studied in COPD of which C-reactive protein (CRP) and fibrinogen are very important. The link between increased CRP and the prediction of cardiovascular risk has suggested that there might be an association between COPD and the increased incidence of cardiovascular disease (CVD) among other comorbidities.<sup>5,6</sup>

Statins are a group of drugs that has shown to have pleiotropic effects like anti-inflammatory and vasodilatory functions in addition to their lipid-lowering effects.<sup>7</sup> Statin therapy has been shown to reduce CRP levels even in those with normal lipid levels. Though proven in coronary artery disease the role of statins in COPD is emerging.<sup>8</sup>

The present study was done to study the relationship between the biomarker of systemic inflammation *viz.* CRP and disease severity, functional status and outcome in COPD patients over a period of 120 days after an acute exacerbation.

## MATERIALS AND METHODS

An observational cross-sectional study was done on 179 patients with COPD presenting in acute exacerbation (AECOPD) to Department of Medicine in Nehru Chikitsalay of B. R. D Medical College, Gorakhpur from January 2014 to June 2014, who were diagnosed by following.

A written Informed consent and Institutional Medical Ethical Committee approval was taken before starting the study.

About 179 patients clinically diagnosed as AECOPD were included in the study. Without any history of diabetes, hypertension and chronic kidney disease, and not consent.

A record was maintained for height, weight, body mass index (BMI), and 6 min walk distance for all patients. Act of three subjected to routine blood examination hemoglobin forced expiratory volume (FEV1) was noted in all patients a spirometry following the (American thoracic guidelines). Modified Medical Research Council Dyspnea Scale was used to assess the severity of dyspnea in COPD patients as per the prescribed format by GOLD.

BODE index for COPD which includes BMI (B), degree of airflow obstruction (O), functional dyspnea (D), and exercise capacity (E) was also obtained from the patient's data. COPD assessment test (CATest) was used to assess the impact of COPD on the functional status of the patient.

All the patients underwent a detail history and clinical examination at presentation and on follow-up visits on days 15, 30, and 120.

## RESULTS

In present cross-sectional study out of 179 patients, 105 (58.65%) were male and 74 (41.34%) were female. Most of the patients were in the age group of 50 to 70 years (60.88%) (mean  $\pm$  50 years).

Comparison of mean CRP levels done by Mann-Whitney test showed that mean CRP among males was  $29.07 \pm 42.07$  mg/l and that in females were  $39.05 \pm 63.05$  mg/l ( $P = 0.93$ ).

The CRP was raised ( $\geq 3$  mg/l) in 136 (75.97%) patients out of that 82 (79.61%) attended day 120 follow-up and the other, 43 (24.02%) patients drop out to some cause. Out of 27 patients who expired, 26 (96.29%) had raised CRP ( $\geq 3$  mg/l) at initial presentation. A total contraindictory 28 patients were lost during follow-up.

The mean CRP of the patients who had raised CRP at the acute exacerbation was  $34.55 \pm 47.18$  mg/l. At 120 days follow-up visit, COPD patients still had a high CRP ( $\geq 3$  mg/l). Mean CRP was  $3.96 \pm 3.69$  mg/l.

Comparison of percentage predicted FEV1 (day 15 follow-up visit) levels in patients with CRP  $\geq 3$  mg/l and those with CRP  $< 3$  mg/l showed that patients with serum CRP levels  $\geq 3$  mg/l had significantly less FEV1 at day 15 follow-up visit than those with CRP  $< 3$  mg/l at presentation.

Mean 6 min walk distance (at day 15 follow-up visit) in patients with CRP  $\geq 3$  mg/l was  $317.92 \pm 91.8$  and those with CRP  $< 3$  mg/l was  $276.3 \pm 102.7$  which means patients with serum CRP levels  $\geq 3$  mg/l had significantly less 6 min walk distance at day 15 follow-up visit than those with CRP  $< 3$  mg/l at presentation.

Median Modified Medical Research Council (MMRC) in patients (109) with CRP  $\geq 3$  mg/l was 3 and patients (43) with CRP  $< 3$  mg/l was 2 which means patients with serum CRP levels  $\geq 3$  mg/l had significantly worse MMRC dyspnea score than those with CRP  $< 3$  mg/l at presentation.

CATest score in patients (109) with CRP  $\geq 3$  mg/l was 24 and those with CRP  $< 3$  mg/l CATest score was 21 which means patients with serum CRP levels  $\geq 3$  mg/l had significantly worse CATest score dyspnea score than those with CRP  $< 3$  mg/l at presentation.

Correlation of change in CRP with change in 6 min walk distance, FEV<sub>1</sub>, MMRC and CATest score over 120 days showed that The change of CRP was significantly correlated with improvement in 6 min walk distance, FEV<sub>1</sub>, MMRC, and CATest score over the study period of 120 days.

Out of those who had raised CRP at day 1 and attended day 120 follow-up visit, 44 patients had CRP ≥3 mg/l and 36 patients had CRP < 3 mg/l at the day 120 follow-up visit.

Expired patients (27) had mean CRP (mg/l) of 45.89 ± 48.93 and Survived (110) patients had CRP (mg/l) of 25.4 ± 3.4 which means The COPD patients who expired during the post exacerbation period had a higher CRP at the acute exacerbation than those who survived. None of the patients who expired were on statin therapy.

Mean CRP at day 1 and day 15 among patients who expired during the study was 45.89 ± 48.93 and 53.98 ± 45.65, respectively, and in those who survived was 25.32 ± 42.66 and 7.98 ± 10.35, respectively.

## DISCUSSION

COPD is a life threatening disease with ever increasing incidence and prevalence. It has been called to be a “Silent epidemic” across the globe. COPD is frequently associated with comorbidities like CVD, osteoporosis, anemia, depression, lung cancer among others which make their impact on health even more alarming.<sup>1,4</sup>

In a study done by Gupta *et al.*, the mean age of COPD patients was 59.38 ± 11.70 years with a Male:Female ratio of 81:19. Our study has shown the similar results.<sup>9</sup>

We enrolled the patients as per the inclusion criteria, and follow-up was advised to them on days 15, 30 and 120 after the initial presentation. At the initial presentation, the mean CRP of all COPD patients was raised in COPD in acute exacerbation. This supports that there is evident systemic inflammation at the acute exacerbation of COPD. The rise in CRP at the exacerbation could be due to a response to infection as there was a group of 43 patients who had CRP <3 mg/l at the acute exacerbation.

The decline in CRP levels on follow-up may be a marker of recovery from the exacerbation of COPD among this subgroup of patients.

Among COPD patients who had CRP <3 mg/l at the initial presentation, there was no significant change in CRP on successive follow-up visits thereafter. This suggests that COPD is a heterogenous disease with multiple phenotypes. Gupta *et al.* did a study in Rohtak and found that that CRP was raised at acute exacerbation of COPD and there was a significant decline in CRP on a follow-up visit thereafter.<sup>9</sup>

We compared the pre-exacerbation functional status among those with raised CRP (≥ 3 mg/l) and those with CRP (< 3 mg/l) at the acute exacerbation. We found that the group of patients with raised CRP had a worse MMRC score and CATest score. They also had a worse FEV<sub>1</sub> and 6 min walk distance at the first follow-up visits.

On interquartile analysis of the lung function parameters, we found that the quartile with higher CRP had a statistically worse CATest score and worse FEV<sub>1</sub> and worse 6 min walk distance at day 15 follow-up visits (Table 1). This further supports that patients with more systemic inflammation had worse functional capacity and more severe airflow limitation. Table 2 showed correlation between CRP with lung function parameters of survivors on corresponding visits.

**Table 2: Correlation analysis between CRP with lung function parameters of survivors on corresponding visits**

LFP	Day 1 (n=109)		Day 15 (n=101)		Day 30 (n=86)		Day 120 (n=80)	
	r	P value	r	P value	r	P value	r	P value
6 MWD	-	-	-0.24	0.003	-0.28	0.002	-0.33	0.0006
FEV <sub>1</sub>	-	-	-0.25	0.002	-0.24	0.01	-0.22	0.02
BODE	-	-	0.4	0.0001	0.23	0.01	0.35	0.0002
MMRC	0.41	0.0001	0.36	0.0001	0.31	0.0008	0.4	0.0001
CAT	0.42	0.0001	0.41	0.0001	0.37	0.0001	0.4	0.0001

CRP: C-reactive protein, 6 MWD (m): 6 min walk distance, MMRC: Modified Medical Research Council Dyspnea Scale, CAT: COPD assessment test, FEV<sub>1</sub>: Forced expiratory volume in 1 s, LFP: Lung Function Parameters. CRP was significantly correlated with 6 min walk distance, FEV<sub>1</sub>, MMRC and CATest score on each of the visits. (r=Pearson/spearman correlation coefficient)

**Table 1: Inter quartile analysis of CRP with respect to various lung function parameters**

Lung function parameter	CRP (mg/l)				P value
	I Quartile (0.2-2.6)	II Quartile (2.6-9)	III Quartile (9-26)	IV Quartile (26-212)	
	(n=39)	(n=37)	(n=37)	(n=37)	
6 MWD (m)	92.4±97.6	263.8±104.5	241.7±99.2	202.4±109.3	0.001
MMRC	2	3	3	3	0.56
CAT	21	22	23	25.5	0.001
FEV <sub>1</sub> (% predicted)	44.5±17.2	2.16±15.1	38.9±14.2	34.6±13.6	0.001

CRP: C-reactive protein, 6 MWD (m): 6 min walk distance, MMRC: Modified Medical Research Council Dyspnea Scale, CAT: COPD assessment test, FEV<sub>1</sub>: Forced expiratory volume in 1 s. With a higher CRP quartile, we observed a worse 6 min walk distance, worse FEV<sub>1</sub> and a worse COPD assessment test score

**Table 3: Comparison of lung function parameters between statin and non-statin group**

LFP	Day 1			Day 30			Day 120		
	Statin (n=30)	Not statin (n=109)	P value	Statin (n=26)	Not statin (n=86)	P value	Statin (n=23)	Not statin (n=82)	P value
CRP	40.7±8.7	31.92±4.2	0.2	5.29±0.9	5.746±0.8	0.7	3.548±0.6577	3.973±0.4718	0.6
6 MWD	254.2±20.6	234.5±9.4	0.4	300.6±18.8	304.7±1.1	0.8	312.7±20.84	317.9±10.92	0.8
FEV <sub>1</sub>	37.96±2.7	37.84±1.3	0.9	38.81±2.7	39.80±1.5	0.7	38.40±2.941	40.89±1.508	0.4
CAT	23	23	0.8	19	18	0.9	17	16	0.9
MMRC	3	3	0.7	2	2	0.6	2	2	0.57

CRP: C-reactive protein, 6 MWD (m): 6 min walk distance, MMRC: Modified Medical Research Council Dyspnea Scale, CAT: COPD assessment test, FEV<sub>1</sub>: Forced expiratory volume in 1 s, LFP: Lung Function Parameters

de Torres *et al.* compared the clinical parameters of COPD patients with initial CRP values >3 mg/l or ≤3 mg/l in a study, and they did not find any significant differences in FEV<sub>1</sub>, forced vital capacity, confidence interval/conventional physiotherapy, GOLD stage, MMRC scale or BODE score between the two subgroups.<sup>10</sup>

In our study, on the last follow-up visit at 120 days after the initial presentation in the stable phase of the disease, COPD patients still had a raised CRP with the mean of 3.96 ± 3.67 mg/l, being higher than 3 mg/l considered as the upper limit<sup>11</sup> denoting a parallel low grade systemic inflammation. This suggests that systemic inflammation is an inherent part of the disease both in the acute exacerbation as well as in the stable state. The ongoing systemic inflammation in COPD may be the link between COPD and the comorbidities often observed in COPD though further studies are required in this regard.

Halvani *et al.* did a study on 45 stable COPD patients and found that CRP was raised in COPD patients without potential confounders like ischemic heart disease and cigarette smoking.<sup>12</sup>

Although present study did not find any benefit of statin in all patients of COPD (Table 3), the role of statins in acute exacerbation of COPD in patients with raised CRP will need to be studied in a larger prospective study.

Our study had some limitations. First, a significant number of patients did not turn up for follow-up at all the visit. Second, we used a turbidimetry method for measurement of CRP and not the enzyme-linked immunosorbent assay method which is said to be the best method.<sup>13</sup>

## CONCLUSION

Present study showed that not all COPD patients had a raised CRP but in those who had a raised CRP, its levels

correlated with lung function and functional status of the individual and CRP trends could be a predictor of death. In our study, we found a definite correlation between CRP and lung function. COPD is the “cause or effect” of systemic inflammation still needs to be established.

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# Lymph Node Lesions in Underserved Population of Andhra Pradesh: A Prospective Study

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## Abstract

**Background:** Lymphadenopathy is of great clinical significance, and the underlying cause may range from a treatable infectious etiology to malignant neoplasms. In literature, there are few documented studies regarding the spectrum of lesions in the underserved population. These lesions can be easily diagnosed on cytology without surgical intervention and appropriately treated.

**Aim of the Study:** To know the various causes of lymphadenopathy in the rural and tribal population of Andhra Pradesh.

**Material and Methods:** The patients with superficial lymphadenopathy attending the outpatient clinics of tertiary care center catering to the needs of the rural and tribal population were subjected to fine-needle aspiration followed by biopsy. The results were analyzed.

**Results:** The spectrum of lesions was: Non-specific lymphadenitis (47.3%), acute suppurative lymphadenitis (3.60%), tuberculous lymphadenitis (28.54%), granulomatous lymphadenitis (7.21%), metastatic carcinoma (3.52%), and lymphoproliferative lesions (1.55%). Overall correlation on cytology was 91.3%, diagnostic accuracy; 97.2%, sensitivity; 100%, and specificity; 94%.

**Conclusion:** The commonest lesion in the underserved was non-specific lymphadenitis and tuberculous lymphadenitis which can be easily diagnosed on cytology and are treatable.

**Key words:** Lymphadenopathy, Non-neoplastic lesions, Neoplastic lesions, Prevalence, Underserved

## INTRODUCTION

Lymphadenopathy is one of the commonest clinical presentations of patients, attending the outpatient department. Etiology varies from an inflammatory process to a malignant condition. There are few documented studies in the underserved population in literature. Lesions of lymph node can be easily diagnosed on fine-needle aspiration cytology (FNAC) but needs expertise. It is a simple, easy technique and reports can be made available within an hour. FNAC has become an integral part of the initial diagnosis and management of patients presenting with lymphadenopathy. This simple technique has recently

gained wide acceptance since it offers a high degree of accuracy, lending itself to outpatient diagnosis and thus making considerable savings in the cost of hospitalization. The present study is conducted at a tertiary care center which caters to the need of tribal, rural and semi-urban population.

## MATERIALS AND METHODS

This prospective study based on a sample of patients who attended the outpatient clinics of tertiary care center from June 2013 to June 2015. Their chief complaints were enlarged superficial lymphadenopathy. FNA was performed using a 10-20 cm disposable syringe attached to a 22-gauge needle. The needle was allowed to move back and forth into different parts of the enlarged lymph node, several times before withdrawal. Aspirates were smeared which was fixed by Isopropyl alcohol to be stained with H and E and air dried smears by May-Grünwald Giemsa. With respect to surgical specimens, they were routinely processed and stained with H and E.

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## RESULTS

Total no of lymphoid aspirates analyzed on cytology were 1219. Cases available for cyto-histopathological correlation were 115. The cases were divided into 6 groups on cytology: Non-specific lymphadenitis - 583(47.3%), acute suppurative lymphadenitis - 44 (3.60%), tuberculous lymphadenitis - 348 (28.54%), granulomatous lymphadenitis - 88 (7.21%), metastatic carcinoma - 43 (3.52%), and lymphoproliferative lesions - 19 (1.55%). Male:Female ratio there was equal incidence. Lymphadenopathy was more common in the age group <20 years (Table 1). A cervical group of lymph nodes were most commonly involved (Table 2). Clinico-histopathological correlation was seen a maximum in tuberculous lymphadenitis (Figure 1). The cyto-histopathological correlation was 100% in malignant lesions (Figure 2). Deferred cases on cytology were eight in number. Four cases of granulomatous lymphadenitis on cytology showed fungal granulomas on histopathology. Four cases of non-specific lymphadenitis turned out to be tuberculous lymphadenitis on histopathology. Overall correlation on cytology was 91.3%, diagnostic accuracy; 97.2%, sensitivity; 100%, and specificity; 94%

## DISCUSSION

Sharma *et al.*<sup>1</sup> analyzed 736 cases of lymphadenopathy in the rural population of Haryana. The most frequent cause of lymphadenopathy was tuberculosis (56.92%) followed by reactive lymphadenitis (26.22%) and metastatic lymphadenopathy (6.38%). A diagnosis of lymphoproliferative disorder was rendered in 2.71% of cases. FNAC was helpful in establishing the diagnosis in 98.65% of the cases.

In the study by Haque and Talukder,<sup>2</sup> the commonest lesions were granulomatous inflammation (40.35%),

chronic non-specific lymphadenitis (27.19%), metastatic carcinoma (17.54%), non-Hodgkin's lymphoma (5.26%), tubercular lymphadenitis (3.51%), acute non-specific lymphadenitis (2.63%), and Hodgkin's lymphoma in 2.63%. Sensitivity and specificity of FNAC were 82.76% and 97.92%.

Gunvanti *et al.*<sup>3</sup> analyzed 70 cases with cervical lymphadenopathy, 41 were males and 29 were females with male preponderance. Among the diagnostic outcome, 34.28% were having tuberculous lesions followed by 24.28% of reactive hyperplasia, 21.43% of secondary metastases, 11.43% of lymphoma, and 7.15% of acute non-specific lymphadenitis. Paliwal and Nigam<sup>4</sup> studied 280 cases of cervical lymphadenopathy. The best diagnostic accuracy on cyto-histological correlation was in cases of metastatic carcinoma (100%) followed by tuberculous lymphadenitis (76.7%) and reactive hyperplasia (75%).

Rajbhandari *et al.*<sup>5</sup> observed reactive lymphadenitis (15), tuberculosis (5), metastatic adenocarcinoma (2), Hodgkin's lymphoma (1), and non-Hodgkin's lymphoma (6) with a sensitivity, specificity, and accuracy rate of 82.7%, 96%, and 88.76%, respectively.

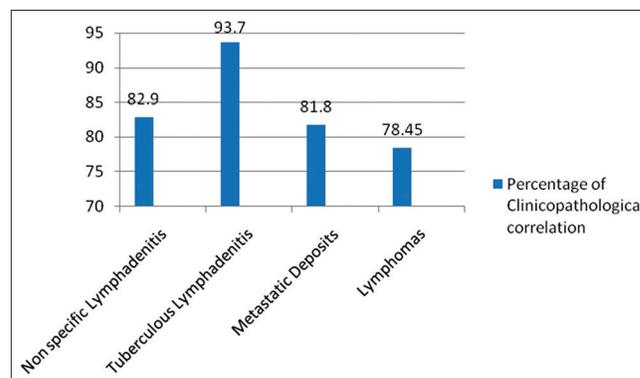
Vidya and Subramanya<sup>6</sup> out of the total 678 cases, most of the cases were in the age group of 20-29 years, with a

**Table 1: Age distribution of various lymphoid lesions on cytology**

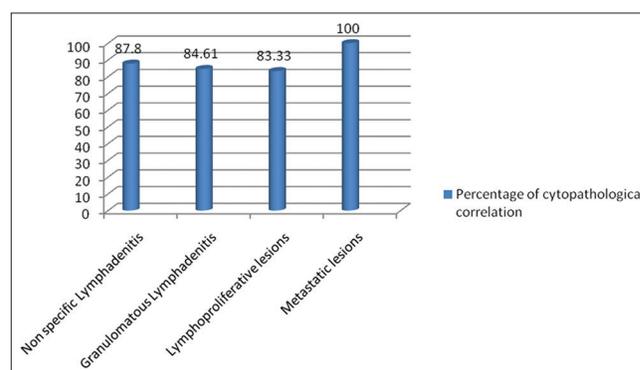
Age distribution (years)	Percentage
<20	37.24
21-40	31.74
41-60	18.12
>60	12.87

**Table 2: Commonest site of lymphadenopathy**

Commonest site	Percentage
Cervical group	62.9
Axillary	18.5
Submandibular	7.4
Supraclavicular	2.22
Inguinal	8.88



**Figure 1: Clinico pathological correlation**



**Figure 2: Cyto pathological correlation**

male preponderance. The most commonly involved were the cervical group of nodes. In benign lymphadenopathies, most of the cases were reactive lymphadenitis (50.44%). Metastatic deposits were seen in 12.68% of cases. Most common subtypes were poorly differentiated carcinoma. 17 cases were diagnosed as Lymphomas, of which 10 were Hodgkin's lymphoma, and 7 were Non-Hodgkin's. Histopathological data was available for 41 cases. 38 cases correlated well with FNAC. There was a good correlation between FNAC and histopathology with an overall agreement of 92.7% (38 out of 41). Considering histopathology as gold standard and specificity of FNAC was 92.7%.

Singal *et al.*<sup>7</sup> of 139 cases of lymph nodal lesions analyzed, 34.53% cases were diagnosed as reactive lymphadenitis, 12.94% of acute inflammatory pathology and metastatic lesions in 30.93% of cases, all were confirmed on histopathology. Among the malignant lesions, metastatic lesions were highest which included mainly metastatic squamous cell carcinoma.

Ghartimagar *et al.*<sup>8</sup> analyzed 508 cases of lymphadenopathy: Reactive or infective cause was seen in 68%, positive for metastasis in 18%, and hematolymphoid malignancies in 2%. The most common site was anterior and posterior triangles cervical nodes. The most common malignancy was adenocarcinoma (67%), followed by metastatic squamous cells carcinoma (15%).

Mustafa *et al.*<sup>9</sup> documented that most common metastatic tumor was metastatic squamous cell carcinoma (51.85%), followed by metastatic adenocarcinoma (7.41%). The sensitivity and specificity of FNAC came out to be 97.37% and 93.75%, respectively, with an overall diagnostic accuracy of 96.29%.

Wilkinson *et al.*<sup>10</sup> reported malignancy in 15.4% of the lymph node aspirates. Sheikh and Parmar<sup>11</sup> in their study, the majority of cytological diagnosis made on the lymph node aspirates were metastasis from squamous cell carcinoma followed by metastasis from ductal carcinoma of breast. In lymphoma, two cases were diagnosed as Hodgkin's lymphoma.

Shrivastav *et al.*<sup>12</sup> documented reactive hyperplasia in (52.38%), tubercular lymphadenitis in (46.21%), and metastatic carcinoma in (56.33%).

Hirachand<sup>13</sup> observed reactive hyperplasia in (41.55%), tubercular lymphadenitis in (28%), metastatic carcinoma in (12.3%), granulomatous lymphadenitis in (9.2%), lymphoma (6%), and suppurative lymphadenitis in (3%). Overall diagnostic accuracy was 92.85% in tubercular

lymphadenitis. In metastatic carcinoma to lymph nodes, sensitivity and specificity of FNAC were 100% each.

In the present study, benign lymphadenopathy constituted a significant proportion of lesions, and malignant lesions constituted 5.07%. The spectrum of lesions was non-specific lymphadenitis (47.3%), acute suppurative lymphadenitis (3.60%), tuberculous lymphadenitis (28.54%), granulomatous lymphadenitis (7.21%), metastatic carcinoma (3.52%), and lymphoproliferative lesions (1.55%). In our series, male to female ration was equal and cervical lymphadenopathy (62.9%) was the commonest.

In the present study, tuberculous lymphadenitis constituted 28.54% and granulomatous lymphadenitis probably due to tuberculosis or other causes constituted 6.89%. Except for 2 cases with fungal granulomas in diabetics, the rest of the cases with diagnosis of granulomatous lymphadenitis on cytology turned out to be tuberculous lymphadenitis on histopathology with a diagnostic accuracy of 84.61%. Out of 19 cases with a diagnosis of the lymphoproliferative lesion on cytology, 18 were confirmed on histopathology as lymphomas with overall diagnostic accuracy of 83.33%. 12 cases were non-Hodgkin's lymphoma, and 3 cases were Hodgkin's lymphoma. Three cases did not correlate; they turned out to non-specific lymphadenitis on histopathology.

The accuracy of FNA in diagnosing metastatic tumors was 100%. Squamous cell carcinoma was the most common type; 60.5%, adenocarcinoma; 15.31%, poorly differentiated carcinoma; 10.21%, papillary carcinoma of the thyroid; 10.9%, and malignant melanoma 2.9%. Sensitivity and specificity of FNAC in the present study were 100% and 94%, respectively.

## CONCLUSION

In the present study, the commonest lesions in the underserved were tuberculous lymphadenitis (28.54%) which can be easily diagnosed on cytology. In malignant lymphadenopathy, 7.21% were metastatic lesions and 1.55% were lymphomas which can be easily differentiated on cytology. FNAC can be easily performed at the primary health center avoiding unnecessary surgery and instituting early therapy.

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# A Clinico-histopathological Study of Psoriasis

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## Abstract

**Background:** Psoriasis is a common disease of unknown etiology, worldwide in distribution affecting men and women of all ages, races, and social strata.

**Aim:** To study various clinical presentations of psoriasis, and to study the histopathological features in various clinical forms.

**Methods:** A 100 consecutive patients with psoriasis, who attended the out-patient department, were selected for the study. A detailed clinical history and a complete general physical examination were done, and the findings were recorded.

**Results:** Psoriasis accounted for 1.2% of the total dermatology outpatients during the period of 2-year from July 2002 to June 2004. Chronic plaque type was seen in 83% of cases, followed by guttate type in 8% of cases. Considering only Munro-microabscesses and Spongiform pustules of Kogoj to be truly diagnostic, only 25% showed definitive evidence of psoriasis. The Most common clinical type of psoriasis remains to be chronic plaque type. Though most of the biopsy specimen showed histopathological features suggestive of psoriasis, only a few specimens showed diagnostic features, i.e., Munro-microabscesses and spongiform pustules of Kogoj.

**Conclusion:** Because the clinical presentations of psoriasis are varied, the definitive diagnosis may depend on the histological examination. However, the histological changes of psoriasis are as varied as the clinical presentations. Therefore, a combination of clinical and histopathological features must be present for the diagnosis of psoriasis to be made in doubtful cases.

**Key words:** Histopathology, Parakeratosis, Psoriasis

## INTRODUCTION

Psoriasis is a common disease of unknown etiology characterized by well-defined erythematous papules and plaques surmounted by silvery white scales over the elbows, knees, scalp, and extensor surfaces. It is a chronic disease marked by periods of remissions and exacerbations.<sup>1</sup> The disease has worldwide distribution and affects men and women of all ages, races, and social strata. Psoriasis is a multifactorial disorder and has a polygenic inheritance.<sup>2,3</sup> It is often believed to be initiated or exacerbated by stressful life event and is extremely variable in its duration and

course.<sup>4,5</sup> Some patients are never completely free of the disease, whereas others experience long-term remission. Typical histological picture is not always found. Despite the advances in pathogenesis, the etiology is yet to be identified. Hence, we conducted a clinical and histopathological study among 100 patients clinically diagnosed as psoriasis.

## METHODS

The 100 consecutive patients with psoriasis who attended the outpatient department for a period of 2-year were included. Patients unwilling for biopsy, those with systemic illness and pregnant women were excluded. A detailed clinical history with special references to age, site of onset, past treatment, seasonal variation, triggering factors, family history of disease, other systemic diseases, and habits were noted. General physical examination, detailed mucocutaneous, and systemic examination were done and the findings were recorded. Skin biopsy was done in all the patients for histopathological studies.

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## RESULTS

Psoriasis accounted for 1.2% of total dermatology outpatients. The male to female ratio was 3:1. The high prevalence and onset of disease was seen in the age group between 21 and 30 years. The disease was present for less than a year in 42 patients. Mild, moderate, and severe itching was seen in 37%, 22%, and 32%, respectively.

Half of the study population had seasonal variation with most of them having winter exacerbation. Six patients had familial psoriasis. History of smoking was present in 48% of patients while 33% were alcoholics.

Scalp (40%) was the most common site of onset followed by lower extremities (28%) and trunk (85%). Extremities (lower and upper) (86.5%) were the most common site of involvement followed by trunk (85%) and scalp (75%) (Table 1).

Nail involvement was seen in 75 cases. Pitting was the commonest finding (72%) followed by nail discoloration (46.66%), subungual hyperkeratosis (29.33%) and longitudinal ridging (20%) (Table 2).

Clinically, the most common type of psoriasis was chronic plaque (83%) followed by guttate (8%), palmoplantar (3%), pustular (3%), erythrodermic (2%), and inverse psoriasis (1%) (Table 3).

Koebners phenomenon was seen in 24% of cases and Auspitz sign in 29%. Hypopigmented halo (Woronoffs ring) around the lesions was seen in 24% of cases (Table 4). On histopathological examination following features were seen: Hyperkeratosis (89%), parakeratosis (75%), acanthosis (75%), hypogranulosis (51%), agranulosis (19%), hypergranulosis (16%), normal granular layer (14%), elongation of rete ridges (75%), Munro-micro abscess (58%), spongiform pustules of Kogoj (30%), capillary dilatation (90%) and lymphocytic dermal infiltration (98%). Among the parakeratosis focal was seen in 59.75%, and confluent in 40.25%. Dense lymphocytic infiltration was seen in 5.10%, moderate infiltration in 14.28% and in the majority, i.e., 81.63% mild dermal infiltration (Tables 5 and 6).

## DISCUSSION

Genetic and environmental factors greatly influence the clinical development of psoriasis. This results in wide differences in the prevalence of the disease among different ethnic groups and in different parts of the world. Further, patients with minimal clinical manifestations often do not seek medical attention. Most studies on prevalence

**Table 1: Sites of involvement**

Site	Number of patients	Percentage
Scalp	75	75.0
Face and neck	31	31.0
Trunk	85	85.0
Upper extremities	86	86.0
Lower extremities	87	87.0
Palms and soles	12	12.0
Mucous membrane	03	03.0
Periumbilical region	01	01.0
Axilla	01	01.0
Nails	75	75.0

**Table 2: Nail changes**

Nail changes	Number of patients	Percentage
Pitting	54	54.0
Longitudinal ridging	15	15.0
Subungual hyperkeratosis	22	22.0
Yellowish discoloration	34	34.0
Shiny	08	08.0
Onycholysis	02	02.0
Transverse ridges	02	02.0
Normal	25	25.0

**Table 3: Clinical types of psoriasis**

Type	Number of patients	Percentage
Chronic plaque	83	83.0
Guttate	08	08.0
Palmo-plantar	03	03.0
Inverse	01	01.0
Erythrodermic	02	02.0
Generalized pustular	02	02.0
Palmo-plantar pustulosis	01	01.0
Total	100	100

**Table 4: Cutaneous features of psoriasis**

Clinical features	Number of patients	Percentage
Papules	38	38.0
Plaques	82	82.0
Scales	98	98.0
Erythema	76	76.0
Hypopigmented halo	24	24.0
Exfoliation	02	02.0
Pustules	03	03.0
Koebner response	24	24.0
Auspitz sign	29	29.0

are based on information from clinical examinations, interviews, census studies, and mailed questionnaires. Estimates of occurrence of psoriasis in different parts of the world vary from 0.3 to up to more than 2%.<sup>6,7</sup> A few studies that have been performed in India to determine the incidence of psoriasis have been on patients attending the clinics and hospitals.<sup>8,9</sup> Hence, these findings do not reflect the true incidence of psoriasis in the general population.

In our study, psoriasis accounted for 1.2% of the total dermatology out-patients.

Onset of psoriasis is most common in the second to fourth decades of life though it can appear just after birth or in old age.<sup>1</sup> In our study, majority of the patients (47%) had the onset of the disease between 21 and 40 years. Some studies have revealed two peaks in age of onset: An early one at 16-22 years and a later one at 57-60 years.<sup>10,11</sup>

The incidence of psoriasis in adult men and women is usually reported to be about equal.<sup>12,13</sup> However, male to female ratio of psoriasis in different studies from India varied from 2 to 4:1.<sup>8,9,14</sup> The lower incidence observed in females from these parts of world may be due to their being less attentive to health, and occurrence of psoriasis over covered parts. The higher incidence of psoriasis among agriculturists in our study may be related to occupational trauma. Itching is variable in psoriasis.<sup>15</sup> It ranges from complete absence to severe pruritus in the minority of patients. It is more

common in unstable forms. The high prevalence and intensity of itching in our psoriatic population may be partially related to the high ambient temperatures existing in our tropical climate throughout the year.

Most patients experienced worsening of their skin lesions during winter. Presumably the xerosis associated with low humidity in winter months explains in part, the seasonal changes in the activity of psoriasis.<sup>16</sup> High humidity is usually beneficial. Although sunlight is generally beneficial, the small minority of psoriatics is provoked by strong sunlight and suffer summer exacerbations in exposed skin.

Smoking is a known risk factor for the development of psoriasis.<sup>17</sup> An association between psoriasis and alcohol consumption has been noted. Because of social and psychological burden, persons with psoriasis may be at higher risk of alcohol abuse.<sup>18</sup> Alcohol consumption may also lead to reduced therapeutic compliance and may interfere with treatment.<sup>19</sup>

Chronic plaque psoriasis continues to be the major type of psoriasis followed by guttate psoriasis. In our study, erythematous scaly plaques were noted more commonly over extremities, trunk, and scalp, and this could be explained by these areas being more prone for trauma and the same reason holds good for the scalp being the most common site of onset in the majority of patients. Psoriatic arthritis may be under diagnosed because of the fact that symptoms of psoriatic arthritis can be very slight causing little discomfort to the patient so that the condition is never diagnosed and also may be because the criteria for evaluating arthritis differ widely. The incidence of Koebners phenomenon has varied between 20% and 33% in different studies.<sup>20,21</sup> We found Koebners phenomenon in 24 cases. There are limitations to historical ascertainment of the Koebners response. An injury or the development of psoriasis at the site of injury may not be recalled. If recalled, the injury and the time course

**Table 5: Histopathology of psoriasis**

Histopathological findings	Number of patients	Percentage
Hyperkeratosis	89	89.0
Parakeratosis	77	77.0
Focal	46	59.7
Confluent	31	40.2
Acanthosis	75	75.0
Hypogranulosis	51	51.0
Agranulosis	19	19.0
Hypergranulosis	16	16.0
Normal granular layer	14	14.0
Elongation of rete ridges	75	75.0
Munro-micro abscess	58	58.0
Kogoj abscess	30	30.0
Capillary dilatation	90	90.0
Dermal infiltration	98	98.0
Mild	80	81.63
Moderate	14	14.28
Dense	4	5.10

**Table 6: Histopathology of various clinical types of psoriasis**

Histopathology	Clinical type (%)						Total
	Chronic plaque n=83	Guttate n=8	Erythrodermic n=2	Pustular n=3	Palmo-plantar n=3	Inverse n=1	
Hyperkeratosis	73 (89.02)	7 (87.5)	2 (100.0)	3 (100.0)	3 (100.0)	1 (100.0)	89
Parakeratosis	64 (77.10)	6 (75.0)	2 (100.0)	3 (100.0)	2 (66.66)	0	77
Acanthosis	60 (72.28)	7 (87.5)	2 (100.0)	2 (66.66)	3 (100.0)	1 (100.0)	75
Hypogranulosis	46 (55.42)	5 (62.5)	0	0	0	0	51
Agranulosis	13 (15.66)	1 (12.5)	2 (100.0)	3 (100.0)	0	0	19
Hypergranulosis	12 (14.45)	1 (12.5)	0	0	2 (66.66)	1 (100.0)	16
Normal granular layer	12 (14.45)	1 (12.5)	0	0	1 (33.33)	0	14
Elongation of rete ridges	63 (75.90)	5 (62.5)	2 (100.0)	2 (66.66)	2 (66.66)	1 (100.0)	75
Micro-munro abscess	47 (56.62)	5 (62.5)	2 (100.0)	3 (100.0)	1 (33.33)	0	58
Kogoj-abscess	24 (28.91)	1 (12.5)	2 (100.0)	3 (100.0)	0	0	30
Capillary dilatation	76 (91.56)	7 (87.5)	2 (100.0)	3 (100.0)	2 (66.66)	0	90
Dermal infiltration	81 (97.59)	8 (100.0)	2 (100.0)	3 (100.0)	3 (100.0)	1 (100.0)	98

of the resulting psoriasis may not be standardized. A higher incidence of Auspitz sign demonstrated in our study may be because of more cases with acute flare.

The histopathological findings in the present study showed features consistent with psoriasis, but there was disparity between findings of other studies.<sup>22,23</sup> This can be explained on the basis of varying degrees of activity of the disease. It is clear that there is a wide spectrum of histologic change recognizable in psoriatic plaques, even when they have not been subjected to specific treatment and also when the clinical appearance does not deviate from the usual. In guttate psoriasis, lesions showed more pronounced inflammatory infiltrate and mononuclear dermal infiltration was seen in all 8 (100%) patients as compared to 81 (97.59%) in chronic plaque psoriasis. Guttate psoriasis shows more pronounced inflammatory infiltrate as the lesions are usually early or active.<sup>24</sup> Though most of the biopsy specimen showed histopathological features suggestive of psoriasis, only few specimen showed diagnostic features, i.e. Munro-micro abscess and Spongiform pustules of Kogoj, although all the specimen were from clinically diagnosed lesions. This indicates that the entirely typical histological features are found only in a small percentage of biopsy specimen, even if only clinically typical lesions of psoriasis are examined. This also concurs with Cox and Watsons<sup>23</sup> observation that a substantial proportion of clinically active psoriatic plaques lack the classical histologic pattern of the disease. Because the clinical presentation is varied, the definitive diagnosis may sometimes depend on the histologic examination. However, the histological changes of psoriasis are as varied as the clinical presentations. Therefore, a combination of clinical and histopathologic features must be present for the diagnosis of psoriasis to be made in doubtful cases.

## CONCLUSION

Psoriasis is a chronic dermatological disorder with chronic remissions and exacerbations. It is commonly seen in the third and fourth decades with a male preponderance. Cutaneous lesions consisted of well-defined erythematous papules and plaques covered with scales. Hypopigmented halo, Koebner phenomenon, and Auspitz sign were the associated features. In different types and at different stages of psoriasis, the histological manifestations are present in varying degrees, and often it is the combination of these manifestations that helps the clinician and a pathologist, arrive at the diagnosis of psoriasis.

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# Impact of Mutations in Medical Science: A Focus on ErbB2 Gene

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## Abstract

**Introduction:** Epidermal growth factor receptor family of receptor tyrosine kinases plays important roles in the development and severity of many cancers across human populations. Single-nucleotide polymorphisms (SNPs) play a major role in understanding the genetic basis of many complex human diseases. It is still a major challenge to identify the functional SNPs in a disease-related gene.

**Purpose:** To explore possible relationships between genetic mutation and phenotypic variations of ErbB2 gene.

**Materials and Methods:** In present study, different bioinformatics algorithms such as sorting intolerant from tolerant (SIFT), polymorphism phenotyping (PolyPhen), and I-mutant server to predict the impact of these amino acid substitutions on ErbB2 were employed.

**Results:** SIFT analysis resulted in 9 of 109 non-synonymous SNPs (nsSNPs) were predicted to be “damaging” and “possibly damaging,” “probably damaging” and “benign” by PolyPhen program. I-mutant 3.0 results demonstrated that all respective mutations would decrease the overall stability of the protein. The orthologous multiple alignments of nsSNPs with ids namely rs28933368 (E914K), rs193171026 (L46F), rs149937802 (R34W), rs140980495 (R536Q), and rs144533600 (E1244K) showed that all mutations were found to be either conserved or the flanking amino acids showed a low degree of conservation except rs149937802 (R34W) where a high rate of mutation was observed among orthologs, which needs further investigation.

**Conclusion:** Current analysis represents the application of computational tools in understanding functional variation from the perspective of structure, expression, evolution, and phenotype.

**Key words:** Amino acid, Breast cancer, ErbB2, Receptor tyrosine kinase, Single-nucleotide polymorphism

## INTRODUCTION

Breast cancer is the most common cause of cancer in women. The gene is involved in low-level susceptibility to breast cancer is ERBB2 (Heregulin 2 [HER2]). This gene is present on chromosome 17q12-q21, spans 38 kilobases, and comprises 27 coding exons.<sup>1,2</sup> ErbB2 is a member of the epidermal growth factor receptor (EGFR) family of receptor tyrosine kinases, which in humans includes EGFR

(ERBB1), ERBB2, ERBB3, and ERBB4. ErbB receptors are vital in facilitating proliferation and differentiation of cells in the developing embryo as well as in adult tissues. Further, it was conceived that an inappropriate activation might result in the development and callousness of many cancers.<sup>3</sup> Over expression of HER2 is found in 20-30% of human breast cancers and correlates with more aggressive tumors and a poorer prognosis. It was identified that ErbB2/ErbB3 heterodimer represents an important oncogenic unit<sup>4</sup> in breast cancer cell proliferation.

Over expression of the ErbB1 and ErbB2 proteins contributes to the aggressive behavior of malignant tumors originating from the endometrium. The expression levels are considerably higher in malignant ones when compared to benign tumors.<sup>5</sup> Anti-cancer therapies involving a monoclonal antibody targeting HER2, Herceptin (also

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known as trastuzumab), is currently prescribed for breast cancer. Herceptin binds to the juxtamembrane region of HER2, identifying this site as a target for anticancer therapies.<sup>6</sup>

Single-nucleotide polymorphisms (SNPs) are modifications of a single nucleotide (adenine, thymine, cytosine, or guanine) in the genome. Around 90% of all human genetic variations constitute SNPs and the probability reaching every 100-300 bases in the human genome.<sup>7</sup> SNPs were found in both coding and noncoding regions of the genome. Non-synonymous SNPs (nsSNPs) is responsible for nearly half of the known genetic variations related to human disease.<sup>8,9</sup> Functional SNP analysis reported for BRCA1, ABL1, ERBB2, CFTR, and EGFR genes.<sup>10-14</sup>

Although several articles reported the association of SNPs in the ErbB2 gene, computational analysis describing the functional consequences of SNPs presented here. We applied different publicly available computational algorithms, such as sorting intolerant from tolerant (SIFT),<sup>15</sup> polymorphism phenotyping (PolyPhen),<sup>16</sup> and I-mutant 3.0 for protein stability analysis<sup>17</sup> and to identify likely deleterious SNPs which could affect protein function. Almost 80% success achieved with SIFT and PolyPhen in benchmarking studies employing amino acid substitutions<sup>18-20</sup> and the “false negative” and “false positive” error rates of SIFT and PolyPhen<sup>21</sup> is 31%, 20%, and 31%, 9%, respectively. The rationale behind the work is to study the importance of mutations in breast cancer target, ErbB2, in particular.

## MATERIALS AND METHODS

### Data Analysis

In this study, it was observed that many variations exist for ErbB2 gene and demarcation of choosing the correct SNPs was a precarious one.<sup>22</sup> One method was to arrange SNPs as per their structural and functional significance. Instead, gene cards ([www.genecards.org](http://www.genecards.org)) was accessed to identify SNPs, and we compared whether it represents a novel or an existing mutational event using an SNPs-database server.<sup>23,24</sup> Therefore, to check the overall effect of such mutations on structure and functional aspects of protein, SIFT and PolyPhen-2 software were employed.

### SIFT

The SIFT<sup>25</sup> program was used to perform protein conservation analysis and predict the phenotypic effect of amino acid substitutions. SIFT was constructed on the principle that protein evolution is correlated with protein function. Variants that occur at conserved alignment positions are tolerated less than those that

occur at diverse positions.<sup>23</sup> The algorithm constructs a multiple sequence alignment of proteins along with the query sequence of same group. The output comprises alignments of homologous sequences and scores that range from 0.0 to 1.0 to each residue are assigned. The SIFT scores<sup>19</sup> were classified as intolerant (0.00-0.05), potentially intolerant (0.051-0.10), borderline (0.101-0.20), or tolerant (0.201-1.00). The lower the tolerance index (TI) of a particular amino acid substitution, the larger is its likely impact. An nsSNP with a TI score of  $\leq 0.05$  is considered to be deleterious, and a score of  $>0.05$  is considered as tolerant.

### PolyPhen-2

PolyPhen-2<sup>26</sup> is a computational tool that identifies functionally potential nsSNPs in the coding region. The prediction is based on combined features involving phylogenetic, structural, and sequence annotations. For a positional variation of an amino acid, PolyPhen-2 performs the following: (a) The program extracts sequence-based features of the variation from the UniProt database, (b) calculates profile scores for two amino acid variants, (c) calculates the structural parameters, and substituted residue contacts. Based on PolyPhen-2 analysis, the scores represent “benign” (0.00-1.50), “possibly damaging” (1.50-1.99), or “probably damaging” ( $>2.0$ ). The query was submitted as a single mutational event with a chromosome co-ordinate. PolyPhen-2 analyzes several protein structure databases and performs multiple alignments of homologous sequences, and reports the amino acid contact information. Further, the difference between two variants is calculated. High differences in scores signify higher functional impact of a particular amino acid substitution.<sup>27</sup>

### Protein Stability Prediction Analysis by I-mutant

I-mutant version 3.0 was used to predict the changes in protein stability on single-site mutations. The program evaluates the stability change starting from the protein structure or sequence. This program was trained on a dataset derived from ProTherm,<sup>17</sup> the most comprehensive database of protein mutations derived from experimental data. I-mutant is a suite of support vector machine 2 (SVM2) based predictors, integrated into a unique web server<sup>23</sup> at <http://gpcr.biocomp.unibo.it/cgi/predictors/I-Mutant3.0/I-Mutant3.0.cgi>

## RESULTS AND DISCUSSION

Gene ErbB2 with a potential role in breast cancer selected for the study. Out of a total of 1038 SNPs, 109 nsSNPs selected from gene cards database ([www.genecards.org](http://www.genecards.org)). Analysis concerning the amino acid conservation in a protein was performed using the SIFT algorithm that

predicts amino acid substitution and possible impact on protein function. The program does by aligning similar proteins and calculates a score that determines the evolutionary conservation status of an amino acid. All 108 nsSNPs submitted to SIFT and the PolyPhen servers, respectively. From the result, nine nsSNPs were predicted to be damaging by SIFT and “possibly damaging,” “probably damaging,” and “benign” by Polyphen program. The Polyphen program report the position-specific independent count (PSIC) score above of 1.0 is considered to be damaging, the results shown in Table 1. The validity of these algorithms based on the benchmarking studies carried out on “known” deleterious substitutions annotated in databases, such as Swiss-Prot, resulted in successful prediction of over 80% of amino acid substitutions. Experimental studies pertaining to individual proteins have confirmed the accuracy of SIFT and PolyPhen.<sup>19,28,29</sup>

From SIFT, the output data represents that higher the TI, the less will be the functional impact of a particular amino acid substitution and vice versa. From Table 1, it is clear that except SNP rs1801201, all other nsSNPs were classified as “damaging” and showed a deleterious TI score of 0.01-0.04 which possibly could affect the protein function of ErbB2 gene.

The nine nsSNPs that resulted from SIFT were submitted to the PolyPhen server and the amino acid variations at the structural level was determined. Table 1 presents the distribution of the variants by PolyPhen score. PolyPhen scores in this dataset ranged from 1.0 to 0.03. An SNP in a nucleotide sequence changes the respective amino acid and they possibly impact the folding patterns, interaction sites, solubility, or stability of proteins. Therefore, to assess the relationship between genetic and phenotypic variation, it is indeed necessary to verify the structural features of the respective non-synonymous mutations in proteins. The results obtained by the SIFT was found to be correlated well with the results obtained by PolyPhen, as seen in Table 1. Hence, we mapped known disease mutations onto known three-dimensional structure of ErbB2 protein based on PolyPhen score. The nsSNPs with IDs namely rs28933368 (E914K), rs193171026 (L46F), rs149937802 (R34W), rs140980495 (R536Q), and rs144533600 (E1244K) showed a PSIC score >0.9 were selected to perform multiple alignments of mutated amino acids on orthologous ErbB2 family of protein sequences. From analysis, evidence suggests that all mutations are either conserved or the flanking amino acids showed a low degree of conservation (Figure 1).

The mutation region corresponding to E914K as well as flanking regions conserved in all orthologous sequences. However, L46F region showed variation with amino acids V (*Mesocricetus auratus*) and M (*Notophthalmus viridescens*),

respectively, moreover, the flanking amino acids are not much conserved (Figure 1). The mutation R34W region, also observed in other organisms represents variation with amino acids Q, L, A, T, S, respectively. The R536Q and E1244K regions highly conserved in all species except few residue variations in flanking regions of 536 position.

### Changes in Stability Due to Mutation

I-mutant 3.0 results obtained in the analysis demonstrated the change in protein stability with relative free energy due to mutation (Table 2). We submitted independently the protein sequence of nine nsSNPs which predicted to be damaging both using SIFT and PolyPhen programs. The second SVM2 based predictor for protein stability changes on single point amino acid mutation demonstrated that all respective mutations would decrease the overall stability of the protein.

**Table 1: Prediction result of SIFT and PolyPhen programs**

SNP ID	Amino acid substitution	SIFT prediction	TI score	PolyPhen prediction	PSIC score
rs28933368	E914K	Damaging	0.01	Probably damaging	1.000
rs1801201	I654V	Tolerated	0.17	Benign	0.303
rs1136201	I655V	Damaging	0.02	Benign	0.406
rs193171026	L46F	Damaging	0.01	Probably damaging	0.974
rs149937802	R34W	Damaging	0.03	Probably damaging	0.992
rs140980495	R536Q	Damaging	0.01	Probably damaging	1.000
rs55943169	A1216D	Damaging	0.01	Benign	0.028
rs144533600	E1244K	Damaging	0.04	Probably damaging	0.999
rs111611886	D1105N	Damaging	0.01	Possibly damaging	0.791

SIFT result: Score ranges from 0 to 1. The amino acid substitution is predicted damaging if the score is  $\leq 0.05$  and tolerated if the score is  $> 0.05$ . PolyPhen-2 result: Probably damaging (more confident prediction)/possibly damaging (less confident prediction). SIFT: Sorting intolerant from tolerant, PolyPhen: Polymorphism phenotyping, TI: Tolerance index, PSIC: Position-specific independent count

**Table 2: Prediction result of I-mutant software**

ErbB2	SNP ID	Amino acid position	WT	MT	SVM2 stability	DDG value prediction Kcal/mol	RI
	rs28933368	914	E	K	Decrease	-0.70	9
	rs1801201	654	I	V	Decrease	-0.99	7
	rs1136201	655	I	V	Decrease	-1.01	7
	rs193171026	46	L	F	Decrease	-1.00	4
	rs149937802	34	R	W	Decrease	-0.11	3
	rs140980495	536	R	Q	Decrease	-0.72	8
	rs55943169	1216	A	D	Decrease	-0.58	4
	rs144533600	1244	E	K	Decrease	-0.78	8
	rs111611886	1105	D	N	Decrease	-0.82	3

For all the predictions, pH and temperature were selected as 7.0 and 25°C, respectively. WT: Wild type amino acid, MT mutant type amino acid, DDG: DG (new protein)-DG (wild type) in Kcal/mol, DDG<0: Decrease stability, DDG>0: Increase stability, RI: Reliability index, SVM: Support vector machine, SNP: Single-nucleotide polymorphisms, SNP: Single-nucleotide polymorphisms

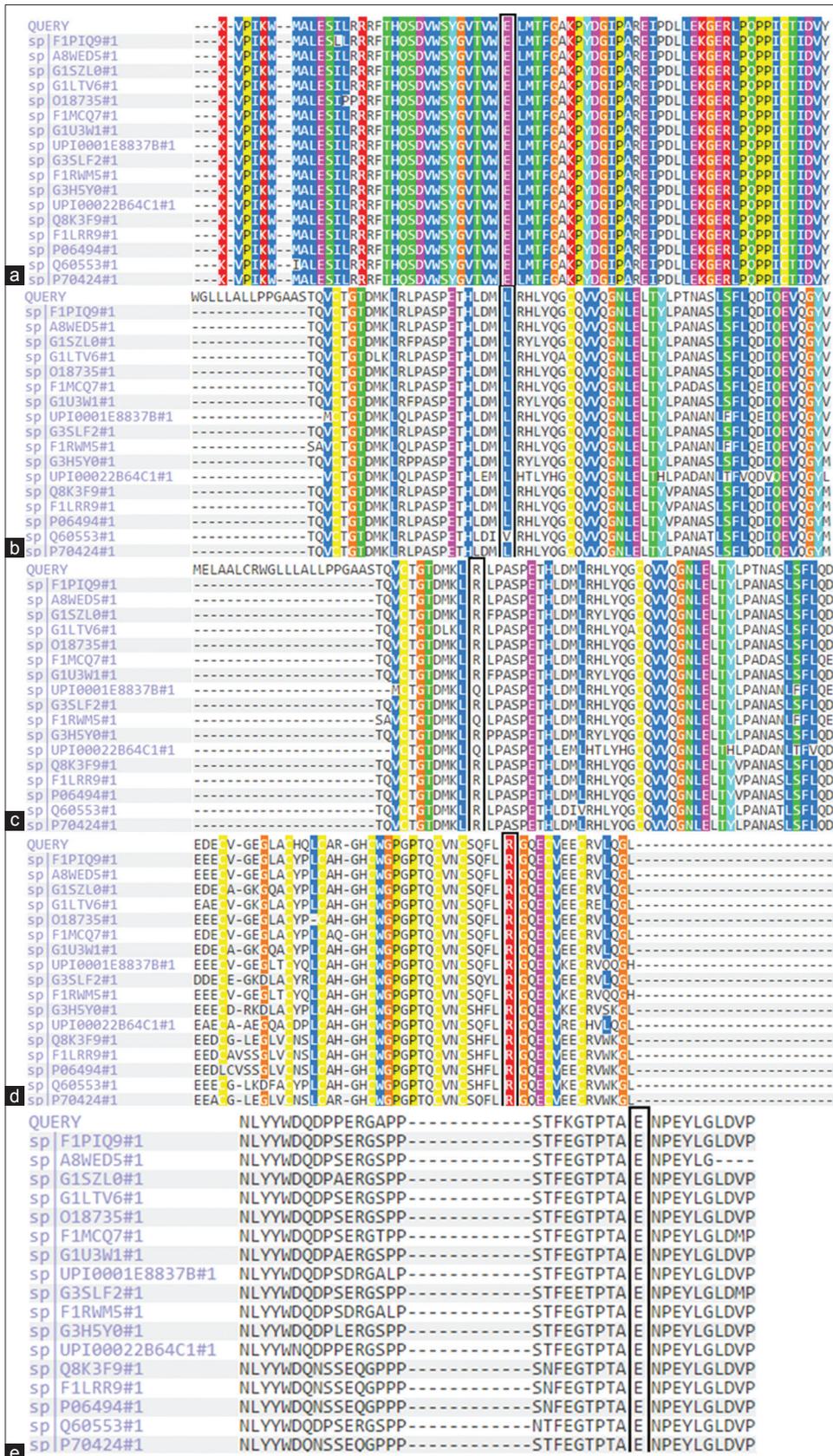


Figure 1: Multiple sequence alignments of non-synonymous single-nucleotide polymorphisms with position-specific independent count score >0.9, (a) E914K, (b) L46F, (c) R34W, (d) R536Q, (e) E1244K

Amino acid substitutions currently account for approximately half of the known gene lesions responsible for human inherited disease.<sup>8</sup> Therefore, the identification of nsSNPs that would probably affect protein function related to a disease is an imperative task in molecular biology. Assessment of nsSNPs based on phylogenetic information (residue conservation) as well as structural approaches, hence, much attention been focused on modeling by different methods. The possible phenotypic variations of SNPs modify amino acids at sequence level thereby affecting the structural parameters, where focus shifted on functional SNPs affecting regulatory regions. Moreover, because of widespread distribution of SNPs on the genome, they have become particularly important and valuable as genetic makers in the research for studying functional loss of proteins and their related pattern on disease susceptibility. Currently, several thousands of human SNPs found by high-throughput methods.

Most molecular studies focused on SNPs located in coding and regulatory regions, yet many of these studies are unable to detect significant associations between SNPs and disease susceptibility. We applied an evolutionary perspective followed by structural approach and mutation stability analysis to SNPs. Moreover, functionally significant amino acids conserved across species; hence SNPs that change the structure and functional features are more likely to be associated with cancer susceptibility. Overall, this analysis will provide useful information in selecting SNPs that are likely to have the potential functional impact on ErbB2.

## CONCLUSION

Current analysis focused on SNPs in the coding regions of ErbB2 enzyme, and the outcome of the study could explain the cancer risk due to the significant fraction of mutational changes to the protein. SIFT analysis resulted in 9 nsSNPs being predicted to be “damaging” and “possibly damaging,” “probably damaging” and “benign” by Polyphen program. These nsSNPs demonstrated a decrease in the overall stability of the protein by I-mutant 3.0 server. Multiple alignments of orthologous nsSNPs, rs28933368 (E914K), rs193171026 (L46F), rs149937802 (R34W), rs140980495 (R536Q), and rs144533600 (E1244K) showed that all mutations were either conserved or the flanking amino acids showed a low degree of conservation except rs149937802 (R34W). On the other hand, a high rate of mutation observed among orthologs. The analysis suggested the application of these software tools and utilizing publicly available databases such as NCBI, dbSNP for analysis resulted in efficient genetic association studies at the molecular level. Our analysis represents the application of computational tools in understanding functional variation

from the perspective of structure, expression, evolution, and phenotype. Further, work is in advancement to evaluate the structural variations of amino acid positions based on PSIC score would highlight the functional and geometrical disturbances in protein structure.

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# Scrotal Calcinosis - An Etiological Dilemma: A Prospective Study

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## Abstract

**Introduction:** Scrotal calcinosis is a rare benign condition of scrotal skin with disputed etiology. It is characterized by single or multiple calcified nodules on a scrotal skin. It should be investigated and confirmed to rule out any malignancy of testis. Fine-needle aspiration cytology is difficult due to calcification. Hence, the only way to confirm is histopathology of excised nodule.

**Purpose:** Purpose of this study was to establish an etiology of scrotal calcinosis.

**Methods:** This is a prospective study over a period of 3-year. The total of 20 patients were analyzed clinically, biochemically, and histopathologically.

**Result:** The total 20 cases of scrotal calcinosis were analyzed, no metabolic, or biochemical abnormalities were found in any of the patient. All cases histopathologically confirmed to be idiopathic in origin.

**Conclusion:** We conclude that scrotal calcinosis is more likely an idiopathic process. Though it is a rare benign disease, such patients should be thoroughly investigated to rule out any hidden pathology.

**Key words:** Idiopathic, Relapsing, Scrotal nodule, Scrotal calcinosis

## INTRODUCTION

Scrotal calcinosis is a rare benign disorder of a scrotal skin. This is characterized by single to multiple painless calcified intradermal nodules of varying size. It was first described by Lewinsky in 1883 as a subgroup of calcinosis cuties. It occurs usually at 20-40 years of age.<sup>1</sup> The condition is mostly asymptomatic, but sometimes patient have complains of heaviness in scrotum, discharge and itching.<sup>2</sup> There is no systemic metabolic disorder. Histological examination reveals extensive deposition of calcium in the dermis. Which may be surrounded by inflammatory cells, histiocytes, and giant cells<sup>3</sup> sometimes a cyst wall is also visible.<sup>4</sup> The exact pathogenesis of scrotal calcinosis is not known. Different authors have given

different opinion which includes dystrophic calcification of epidermal cyst,<sup>4</sup> eccrine duct millia,<sup>5</sup> or dartoic muscle,<sup>6</sup> and calcification secondary to minor trauma of the scrotum.<sup>7</sup> The most studies showed normal serum levels of calcium, phosphorus, and blood sugar. Although this condition is benign, it needs to be differentiated from other benign conditions of the scrotum namely epidermal inclusion cyst, steatocystoma. Definitive diagnosis is based on histology.

## MATERIALS AND METHODS

This is a prospective study of scrotal calcinosis carried out at the department of pathology, government medical college Srikot, Srinagar, Pauri Garhwal, Uttarakhand over a period of 3-year (February 2012-March 2015). All the patients of the scrotal nodules visited in surgical outpatient department were examined clinically, biochemically, and histologically. Only histologically confirmed cases were included in the study. Sample of histopathology was also collected from the surgeries done outside. A total of 20 patients were examined during this period patients of all ages were included in the study. Investigations of patients

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included complete blood count, serum and urinary calcium, phosphorus, fasting, and post-prandial blood sugar levels. Histopathology was done in all cases. Histopathological slides were stained with hematoxylin and eosin stain.

**RESULT**

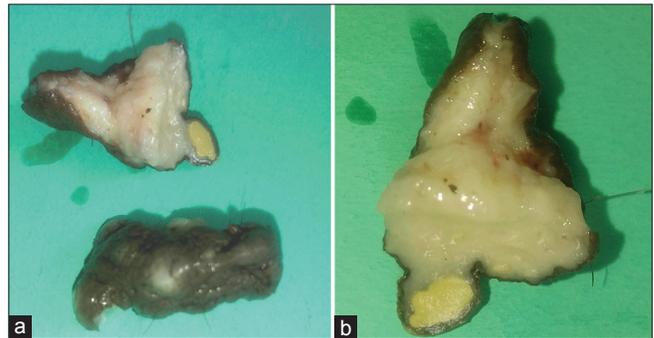
The age of patients ranged from 18 to 70 years (Table 1) with maximum number of patients in the 3<sup>rd</sup> and 4<sup>th</sup> decade. The most common symptom was scrotal nodules (Table 2). No aspiration cytology was done. Biochemical findings were within normal limits. No metabolic abnormality was detected. All specimens of scrotal nodules received for histopathology grossly showed multiple nodules covered with skin (Figure 1a), cut surface showed whitish areas (Figure 1b). Histopathology of all patients scrotal nodule revealed calcified basophilic structure at places separated by fibrous connective tissue (Figure 2a and b) and surrounded by mononuclear inflammatory cells and foreign body giant cells (Figure 3). No cystic structure or capsule was in the slide. On the bases of these features scrotal calcinosis was labeled as idiopathic condition.

**DISCUSSION**

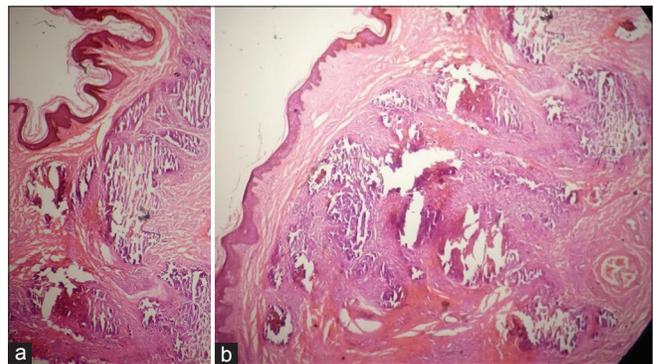
Idiopathic Scrotal calcinosis is a benign condition characterized with calcified deposits surrounded by granulomatous reaction of a foreign body type.<sup>4,8</sup> Clinically, it appears as varying size nodules, solitary or multiple, yellow, hard in consistency. Idiopathic Scrotal calcinosis occurs in the absence of the tissue injury or systemic metabolic disorder. No causative factor has been identifiable. In general, these nodules grow slowly throughout the years and increase in number.

Scrotal calcinosis though commonly seen in the 3<sup>rd</sup> and 4<sup>th</sup> decade of life, but also reported in adult and pediatric

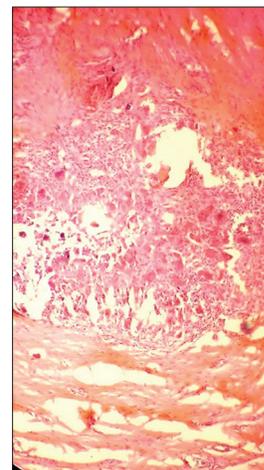
age groups between 9 and 85 years.<sup>9</sup> In our study, common age group was the 3<sup>rd</sup> and 4<sup>th</sup> decade which correlates with literature. Scrotal calcinosis is more common among dark colored race. The most common presentation is scrotal nodule, which do not cause major symptoms. In our study also scrotal nodule was most common complain. The patient usually visits doctor because of cosmetic concern. A few patients may have pruritis, ulceration, and chalky discharge. Clinically, it can be confuse with calcified oncocercoma.<sup>10</sup>



**Figure 1: (a) Gross-skin covered scrotal nodule, (b) cut surface showing whitish areas**



**Figure 2: Photomicrograph showing calcified nodules in dermis. (a) H and E, x10, (b) H and E, x40**



**Figure 3: Photomicrograph showing giant cell and inflammatory cell (H and E x100)**

**Table 1: Age distribution**

Age group	Age in years
0-20	01
21-40	15
41-60	02
61-80	02

**Table 2: Clinical features**

Clinical presentation	Number of patients	Percentage
Symptomless	04	20
Scrotal nodule	15	75
Pruritis	03	15
Chalky white	01	05
Ulceration	None	-

Solitary neurofibroma, ancient schwannomas, steatoma. Histological examination is necessary to differentiate scrotal calcinosis from these lesions.

Pathogenesis of scrotal calcinosis is controversial in this study all the biochemical investigations were within normal limits. These rules out the possibility of metastatic calcification. Hence, this calcification may result due to the presence of pathological lesion (dystrophic calcification) or occur in the absence of a known underlying pathology (idiopathic calcification). On histological examination of our 20 cases, we found calcified basophilic deposits with foreign body giant cell reaction all around (100%), minimal to florid monocyctic, histiocytic inflammatory infiltrate around deposits. Deposits of calcium were separated by fibrous tissue; keratin was not found admixed with these deposits. No cyst or cyst wall was found in any of our case. This indicates towards idiopathic etiology of scrotal calcinosis.<sup>11</sup> Idiopathic etiology was first established by Shapiro *et al.* in 1970 in his study of 35 cases. All immunohistochemical and histopathological studies demonstrate that scrotal calainosis is idiopathic.<sup>12</sup> Some literatures show presence of cyst wall of stratified squamous epithelium.<sup>13</sup>

Recurrence after surgery is not usual in scrotal calcinosis. However, some authors<sup>14,15</sup> have reported recurrence in scrotal calcinosis. In our case, there was no recurrence until 9 months to 3 years of surgery. The good esthetic result was obtained.

## CONCLUSION

Idiopathic scrotal calcinosis is a benign mass with a debatable pathogenesis. Surgical excision is the treatment of

choice, which is required also from an aesthetic perspective. The peak incidence is in the 3<sup>rd</sup> and 4<sup>th</sup> decade which is same as for testicular tumors which has good prognosis if detected early. This makes necessity to investigate all the patients with scrotal nodules.

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# An ImageJ Based Semi-Automated Morphometric Assessment of Nuclei in Oncopathology

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## Abstract

**Introduction:** Nuclear morphology is an important determinant in the diagnostic and prognostic interpretation of tumors. Incorporation of morphometric analysis of the nucleus makes such interpretations more objective and precise. In this study, we have used a semi-automated image analysis method to analyze tumor nuclei in breast and cervical cancer.

**Methods:** Using ImageJ and three of its plug-ins - Kuwahara filter, Bi-exponential edge preserving smoother filter, and Mexican hat filter - We developed an image processing algorithm. We used this to analyze the nuclear parameters in three grades of invasive ductal carcinoma and cervical neoplastic lesions including cervical intraepithelial neoplasia 1 (CIN1), CIN2, carcinoma *in situ* (CIN3), and squamous cell carcinoma. The parameters analyzed were a nuclear area, perimeter, and circularity. The results obtained were statistically analyzed.

**Results:** Mean and standard deviation values of area and perimeter measurements showed statistically significant differences between the three grades of breast carcinoma. Within the cervical neoplasia, there were statistically significant differences between invasive carcinoma and intraepithelial neoplasia of all grades. In addition, median values for area parameter was much lower than mean values suggesting a skewed distribution of tumor cells.

**Conclusions:** This study suggests that morphometric analysis of nuclear parameters is helpful in the grading of the tumors and in assessing their prognosis. In higher grade tumors, the median value for the nuclear area is markedly lower than the mean value suggesting a right skewed distribution. The latter feature may be an important characteristic of aggressive tumors.

**Key words:** Analysis, Breast neoplasms, Carcinoma, Squamous cell, Uterine cervical neoplasms

## INTRODUCTION

In the diagnostic histopathological evaluation of tumors, nuclear morphology plays a central role. The nature of the tumor and its aggressiveness are mainly determined by nuclear features. With the coming of digital age and the easy availability of several image analysis softwares, histomorphometry is being increasingly used in oncopathology for diagnostic, prognostic, and research purposes.<sup>1</sup> Among tumors that have been studied include those of colon, breast, ovary, skin, kidney, etc.<sup>1-4</sup> One of the most popular image analysis softwares is ImageJ,

an open source software developed by Rasband at National Institute of Health.<sup>5</sup> It has a simple interphase and numerous free plugins. In an earlier study,<sup>6</sup> we used ImageJ and three of the plugins, for the first time, to develop an image processing and analysis algorithm to analyze papanicolaou (PAP) smears. In this study, we have modified the processing algorithm to make it capable of analyzing nuclear morphology in histopathological sections. Using that we have analyzed breast carcinoma and cervical neoplasia.

## MATERIALS AND METHODS

Nuclear measurements were carried out on invasive ductal carcinomas of breast of all the three grades and cervical lesions including cervical intraepithelial neoplasia 1 (CIN1), CIN2, CIN3 (carcinoma *in situ* [CIS]), and squamous cell carcinoma. Tissue samples from all these cases were processed to prepare 3 micron sections. These sections

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were stained with hematoxylin and eosin (H and E) stain. Digital images of representative areas were taken using 8 mega pixel Olympus SP 350 compact Zoom Camera attached through a microscope adopter to Olympus CX 41 trinocular microscope. The photographs were taken using  $\times 40$  objective and  $\times 10$  ocular. The images were processed in a photo-editing software to improve the contrast. In all images, three representative areas, each equivalent to  $1600 \times 1200$  pixel crop (1, 92,000 pixels), were used for nuclear analysis. In breast carcinoma, a minimum of 340 nuclei (and up to 1785) were analyzed. In cervical neoplasia, a minimum of 165 nuclei (and up to 441) were analyzed. ImageJ image analysis software was used in this study to carry out nuclear measurements.<sup>5</sup> In an earlier study,<sup>6</sup> we had developed an analysis algorithm using three ImageJ plug-ins to analyze PAP smears: Kuwahara filter,<sup>7</sup> Bi-exponential edge preserving smoother (BEEPS) filter,<sup>8</sup> and Mexican hat filter.<sup>9</sup> That algorithm was modified and adapted to analyze histological sections (Figure 1). The Kuwahara filter reduces the noise and gently homogenizes the area of interest while preserving the edges; BEEPS filter blurs the distracting background without adversely influencing the edges; and the Mexican Hat Filter applies Laplacian of Gaussian filter to isolate signal from the noise.

### Processing Algorithm

After the images were separated into individual colors using color deconvolution plug-in,<sup>10,11</sup> “color one,” which represents hematoxylin component, was selected (when using this plug-in, vector “H and E” was selected). On “color one,” “Kuwahara filter” was applied with sampling window showing an odd number between 5 and 9. BEEPS filter was applied twice (iteration = 2) at the default value. A radius between 3 and 5 was chosen for Mexican hat filter.

The quality of sections (thinner sections yield better results) and the image contrast should be good to ensure optimal results. The “analyze tool” in ImageJ was configured to measure Area, Perimeter, and Circularity. The perimeter is the boundary length of a region of interest (ROI, in this case, is nucleus). Circularity value indicates how close to a circle the object is. The settings for “Analyze tool” were as follows: Size = 1000 to infinity (to exclude structures <1000 pixels); circularity = 0.20-1 (to ignore elliptical and linear structure); show = Overlay outlines or masks. The unit of measurement was pixel (default in ImageJ). Cellular density was calculated for 100000 pixels.

The processing of the images was partially automated by creating two macros. First macro executed the steps from color deconvolution to application of Mexican hat filter; then thresholding and binary conversions were done manually; this was followed by the second macro to execute the final steps of processing and analysis (Figure 2). The report (results and summary) is generated automatically as a spreadsheet.

The results obtained were analyzed statistically. The mean value and standard deviation of different samples were compared using *t*-test (for means) and *F*-test (for standard deviations). A  $P < 0.05$  was taken as significant.

## RESULTS

### Breast Carcinoma

Nuclear density (i.e., number of cells per 100000 pixels) increased with the grade of the tumor: Grade 1 = 59; Grade 2 = 77.4; and Grade 3 = 89.3. More aggressive tumors were associated with higher density (Table 1).

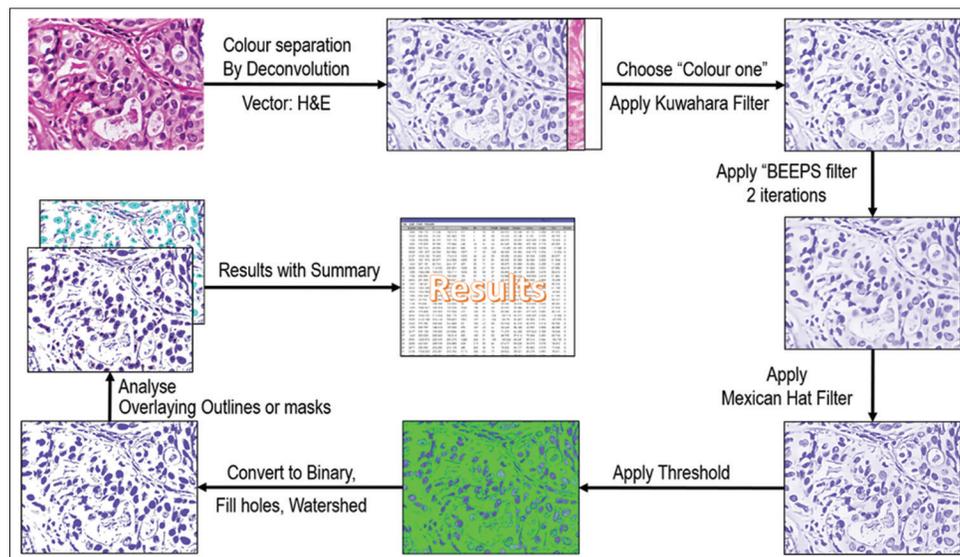


Figure 1: The processing algorithm

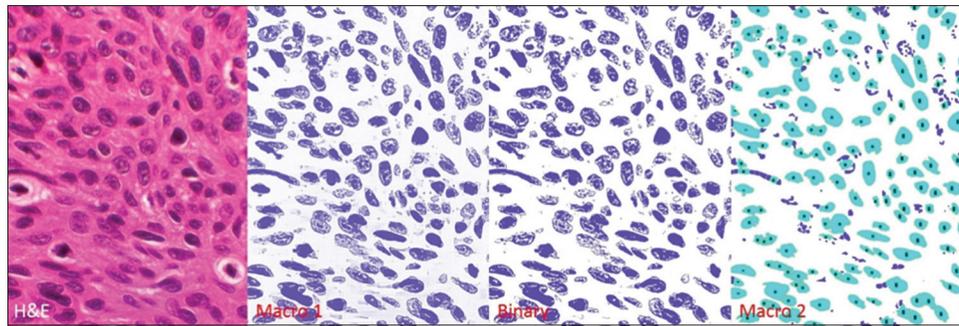


Figure 2: Processing of image analysis was done in three steps involving the application of two macros and manual binary conversion (original H and E image taken at  $\times 40$ ; the image size is  $1600 \times 1200$  pixels)

**Table 1: Mean, median, and SD values for the measured parameters in three grades of breast carcinoma**

Lesion	Count (density)	Mean $\pm$ SD (median)		
		Area	Perimeter	Circularity
Grade 1	340 (59)	1673.24 $\pm$ 581.82 1553.5	180.20 $\pm$ 37.73 175.5095	0.655 $\pm$ 0.138 0.6715
Grade 2	1785 (77.5)	2118.88 $\pm$ 960.65 1912	200.79 $\pm$ 48.18 192.024	0.652 $\pm$ 0.137 0.664
Grade 3	1543 (89.3)	2299.15 $\pm$ 1211.06 1966	211.89 $\pm$ 59.32 201.196	0.635 0.651 $\pm$ 0.142

Count: Number of nuclei counted; Density (in parenthesis in the second column): Number of nuclei/100000 pixels, SD: Standard deviation

**Morphometric Analysis**

Results of nuclear measurements in breast carcinoma and cervical neoplasia are summarized in tables (Tables 1 and 2).

Two of the parameters measured, i.e., area and perimeter showed a very good correlation with the grade of the tumor. The mean, standard deviation (SD) and median values for these two parameters were much higher in grade 3 tumors compared to the tumors of lower grades (Table 1). The differences in mean and SD were statistically significant ( $P < 0.001$ ) (Table 2). These results are consistent with the view that nuclear enlargement and pleomorphism (higher SD) are characteristic of higher grade tumors. There was also a statistically significant difference in the values obtained for these two parameters when we compared Grade 2 tumors to Grade 1 tumors. As far as circularity was concerned, only Grade 3 tumors showed a significantly lower value ( $P < 0.05$  to  $0.01$ ) than the other grades implying that the tumor cells were less circular and more irregular. One other significant observation was that the median value for area parameter was much lower than the mean value suggesting a skewed distribution of tumor cells particularly in tumors of a higher grade.

**Cervical Neoplasia**

Nuclear density varied with the type of the lesion. There was a progressive increase in nuclear density as intraepithelial neoplasia progressed from CIN 1 to CIN3:

**Table 2: Comparison of mean and SD values for the measured parameters within three grades of breast carcinoma with statistical significance**

Parameters	Values	Grade 1	Grade 2	Grade 3
<b>Area</b>				
Grade 1				
Mean	1673.24	-	$P < 0.001$	$P < 0.001$
SD	581.82	-	$P < 0.001$	$P < 0.001$
Grade 2				
Mean	2118.88	$P < 0.001$	-	$P < 0.001$
SD	960.65	$P < 0.001$	-	$P < 0.001$
Grade 3				
Mean	2299.15	$P < 0.001$	$P < 0.001$	-
SD	1211.06	$P < 0.001$	$P < 0.001$	-
<b>Perimeter</b>				
Grade 1				
Mean	180.2	-	$P < 0.001$	$P < 0.001$
SD	37.738	-	$P < 0.001$	$P < 0.001$
Grade 2				
Mean	200.799	$P < 0.001$	-	$P < 0.001$
SD	48.18	$P < 0.001$	-	$P < 0.001$
Grade 3				
Mean	211.89	$P < 0.001$	$P < 0.001$	-
SD	59.32	$P < 0.001$	$P < 0.001$	-
<b>Circularity</b>				
Grade 1				
Mean	0.655	-	$P = 0.815$	$P < 0.05$
SD	0.139	-	$P = 0.727$	$P = 0.571$
Grade 2				
Mean	0.653	$P = 0.815$	-	$P < 0.001$
SD	0.137	$P = 0.727$	-	$P = 0.115$
Grade 3				
Mean	0.635	$P < 0.05$	$P \leq 0.001$	-
SD	0.142	$P = 0.571$	$P = 0.115$	-

SD: Standard deviation

CIN1 = 28.6; CIN2 = 65; and CIN3 = 73. However, full blown squamous cell carcinoma exhibited lower density than CIN 2 and CIN 3:57.4 (Table 3).

The mean and SD of all the measured parameters showed significant differences between squamous cell carcinoma and different types of intraepithelial neoplasia ( $P < 0.05$  to  $0.0001$ ) (Table 4). In addition, the standard deviation of area parameter was markedly high implying a high degree of pleomorphism. The median value for area parameter was much lower than the mean (2245 vs.

3350.99 pixels). This is indicative of markedly skewed distribution of tumor cells. Within intraepithelial neoplasia, the mean values and SD for the area were not significantly different between CIN2 and CIN3 (CIS). However, the values for measured parameters for CIN1 were significantly lower than CIN2 ( $P < 0.05$ ).

## DISCUSSION

Study of nuclear morphology is an important part of the histological evaluation of tumors. Even under routine light microscopic evaluation, nuclear characteristics provide the crucial information necessary to determine the tumor's biological behavior and aggressiveness. With the advent of digital age, image analysis techniques have been increasingly applied to study the nuclear morphology as such evaluations are likely to be less subjective and more precise. Many proprietary (Imagepro Plus,<sup>12</sup> Pax-It,<sup>13</sup> Olympus Stream,<sup>14</sup>) and open source (ImageJ, Cell-Profler,<sup>15</sup>) softwares are available to do the same. Of these, ImageJ is quite popular as it has large number plugins and is relatively simple to use.

In an earlier morphometric study,<sup>6</sup> done on PAP smears, we used three of its plugins (BEEPS, Kuwahara Filter, and Mexican hat filter) in a newly designed algorithm. In the present study, we modified that algorithm to suit the assessment of histological sections. The histological sections, in general, tend to be slightly thicker than cytological smears with cohesive cells dispersed in a distracting stromal background. Besides that, the excessive clumping of chromatin makes nuclei less homogeneous. So, our design goals when developing the processing algorithm were to render the nucleus more homogeneous while preserving its edges and to isolate it from the distracting background. To achieve the former effect, the median filter is commonly used. It achieves homogeneity by softening the details. However, it causes blurring of the edges. So,

we used Kuwahara filter for achieving this. It removes the noise and renders the target area more homogeneous but preserves the edges. Both BEEPS filter and Mexican hat filter help in isolating the ROI in their separate ways; the former blurs the background while preserving the edges; the latter enhances the signal by applying Laplacian of Gaussian filter. Our method worked consistently when the nuclei were well stained with adequate contrast.

Commonly measured parameters include nuclear area, its perimeter, circularity, and diameter. Of these, the diameter is in most cases a derived parameter as most cells/nuclei in histological material are not circular. In the morphometric analysis, the mean and median values of these parameters and the standard deviation (reflecting the extent of

**Table 3: Mean, median, and SD values for the measured parameters in cervical neoplasia including squamous cell carcinoma**

Lesion	Count (density)	Mean±SD (median)		
		Area	Perimeter	Circularity
SCC	441 (57.4)	3350.99±2730.39 2245	274.70±114.27 242.83	0.512±0.132 0.495
CIS				
CIN 3	281 (73)	2877.97±1652.19 2423	232.84±71.10 222.066	0.635±0.103 0.64
CIN 2	252 (65)	2972.76±1521.26 2590.5	238.74±62.76 236.6435	0.631±0.127 0.647
CIN 1	165 (28.6)	2647.85±1246.95 2319	220.74±55.54 213.966	0.666±0.137 0.692

SCC: Squamous cell carcinoma; CIS: Carcinoma *in situ*, CIN 1, 2, 3: Cervical intraepithelial neoplasia 1, 2, 3, Count: Number of nuclei counted, Density (in parenthesis in second column): Number of nuclei/100000 pixels, SD: Standard deviation

**Table 4: Comparison of mean and SD values for the measured parameters within cervical neoplasia including squamous cell carcinoma with statistical significance**

Parameters	Values	SCC	CIS	CIN2	CIN1
Area					
SCC					
Mean	3350.995	-	$P < 0.01$	$P < 0.05$	$P < 0.005$
SD	2730.389	-	$P < 0.001$	$P < 0.001$	$P < 0.001$
CIS					
Mean	2877.968	$P < 0.01$	-	$P = 0.5$	$P = 0.122$
SD	1652.193	$P < 0.001$	-	$P = 0.181$	$P < 0.001$
CIN2					
Mean	2972.766	$P < 0.05$	$P = 0.492$	-	$P < 0.05$
SD	1521.263	$P < 0.001$	$P = 0.181$	-	$P < 0.01$
CIN1					
Mean	2647.855	$P < 0.005$	$P = 0.122$	$P < 0.05$	-
SD	1246.95	$P < 0.001$	$P < 0.001$	$P < 0.01$	-
Perimeter					
SCC					
Mean	274.701	-	$P < 0.001$	$P < 0.001$	$P < 0.001$
SD	114.273	-	$P < 0.001$	$P < 0.001$	$P < 0.001$
CIS					
Mean	232.842	$P < 0.001$	-	$P = 0.312$	$P = 0.061$
SD	71.104	$P < 0.001$	-	$P < 0.05$	$P = 0.001$
CIN2					
Mean	238.747	$P < 0.001$	$P = 0.312$	-	$P < 0.005$
SD	62.763	$P < 0.001$	$P < 0.05$	-	$P = 0.090$
CIN1					
Mean	220.742	$P < 0.001$	$P = 0.061$	$P < 0.005$	-
SD	55.537	$P < 0.001$	$P < 0.001$	$P = 0.090$	-
Circularity					
SCC					
Mean	0.512		$P < 0.001$	$P < 0.001$	$P < 0.001$
SD	0.132		$P < 0.001$	$P = 0.498$	$P = 0.550$
CIS					
Mean	0.635	$P < 0.001$		$P = 0.688$	$P < 0.01$
SD	0.103	$P < 0.001$		$P < 0.001$	$P < 0.001$
CIN2					
Mean	0.631	$P < 0.001$	$P = 0.688$		$P < 0.01$
SD	0.127	$P = 0.498$	$P < 0.001$		$P = 0.280$
CIN1					
Mean	0.666	$P < 0.001$	$P = 0.01$	$P = 0.01$	
SD	0.137	$P = 0.550$	$P < 0.001$	$P = 0.280$	

SCC: Squamous cell carcinoma, CIS: Carcinoma *in situ*, CIN 1, 2, 3: Cervical intraepithelial neoplasia 1, 2, 3, SD: Standard deviation

variation and distribution) are collected. The nuclear area and perimeter measurements have been shown in several studies to have good correlation with prognosis in breast carcinomas,<sup>3</sup> and melanomas.<sup>16</sup> They have also been shown to be useful in distinguishing benign from malignant lesions. Some studies have claimed that standard deviation has a better predictive value than the mean value.<sup>1,16</sup>

In our study, we measured area, perimeter, and circularity. Circularity is a measure of how close to a circle the ROI is. If it is close to 1, the ROI is nearly circular; if it is close to 0, ROI is linear or markedly elliptical. The mean values for the area, perimeter, and standard deviation for the three grades of breast carcinoma showed statistically significant differences. However, the values for circularity did not exhibit statistically significant variation between all the grades.

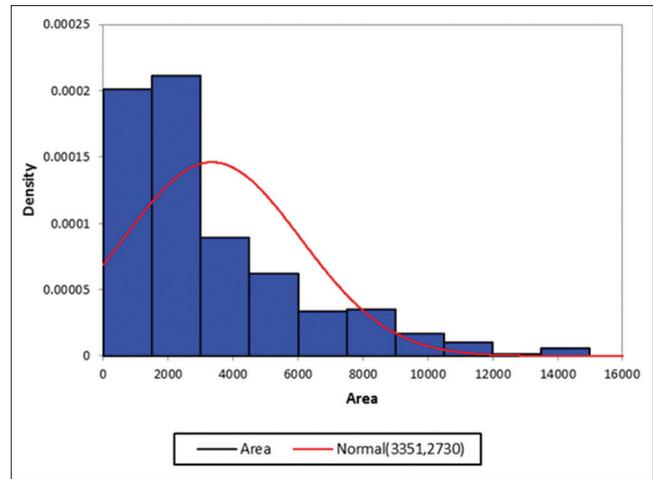
Within cervical neoplasia, morphometry proved extremely useful in differentiating squamous cell carcinoma from cervical intraepithelial neoplasia of all grades. Differences in the means and standard deviations of all the measured parameters (area, perimeter, and circularity) were statistically highly significant. The latter observation is in agreement with the results of an earlier study.<sup>1</sup> Within the intraepithelial neoplastic lesions, only CIN1 showed statistically significant differences with CIN2 and CIN3 in the mean and SD values of the measured parameters. However, differences between CIN2 and CIN3 were not significant. Rightly, the latter two entities should be treated as one (as done in PAP cytology).

We measured median values of all the parameters. There was noticeable to marked differences between the values for median and mean of area parameter. The median values were consistently lower than mean values suggesting a right (positive or upward) skewed distribution. This was borne out when we did distribution fitting (Figure 3). This was more marked in higher grade lesions.

We also determined the nuclear density (number of nuclei/100000 pixels) in all the lesions. In breast carcinoma, nuclear density was much higher in Grade 3 lesions (89.3) compared with lower grade lesions (59 and 77.4) (Table 1). However, among cervical lesions, the highest nuclear density was observed in CIS (CIN3 - 73). Squamous cell carcinoma had much lower nuclear density (57) than CIN2 (65) and CIN3 (Table 3).

## CONCLUSION

A newly designed image analysis algorithm was employed to analyze nuclear morphology in breast and cervical



**Figure 3: Distribution fitting of the results of squamous cell carcinoma showing right (positive or upward) skewed distribution**

carcinomas. The nuclear parameters analyzed include area, perimeter, and circularity. The mean, median, and standard deviations of all the measured parameters were determined. In addition, nuclear density was also found out. The following conclusions were drawn:

- The mean and the standard deviation values of the nuclear area and perimeter showed statistically significant differences between the three grades of breast carcinoma. The nuclear morphometry can be employed usefully in assessing the grade.
- Similarly, there were statistically significant differences between squamous cell carcinoma and all grades of cervical intraepithelial neoplasia.
- The Median values for the area parameter, in particular, was significantly lower than the values for the mean in higher grade lesions including squamous cell carcinoma, suggesting a right skewed distribution. The latter may be an important characteristic of carcinomas and may be used in distinguishing it from benign lesions that mimic carcinoma. However, further observations are necessary.
- The nuclear density showed a direct correlation with the grade of breast carcinoma. In cervical lesions, CIS (CIN3) had the highest nuclear density.

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# Role of Serial Ascitic Fluid Analysis and Other Prognostic Factors in Spontaneous Bacterial Peritonitis

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## Abstract

**Introduction:** Cirrhosis of the liver is one of the commonly encountered liver disorders in clinical practice caused by a wide variety of etiologies. It is defined anatomically as a diffuse process of nodule formation and fibrosis in the liver. Spontaneous bacterial peritonitis (SBP) is defined by infection of the previously sterile ascitic fluid (AF), without any apparent intra-abdominal source of infection. SBP is one of leading cause of death in decompensated liver disease which need prompt diagnosis and treatment. There is increasing toll of alcoholic liver disease, and its complications in Assam in recent times. However, information regarding the clinical profile and bacteriological profile of SBP and its impact on outcome of cirrhotic patients is still lacking in many aspects in this part of the country.

**Aims and Objectives:** This study was undertaken with an idea to evaluate the significance of serial AF analysis and other biochemical markers to determine prognosis in cirrhotic patients in this region.

**Materials and Methods:** Patients admitted with hepatic cirrhosis with ascites were studied during the period from July 2013 to July 2014. All patients included in the study were confirmed hepatic cirrhosis either by liver biopsy or ultrasound with ascites presented with features of the SBP.

**Results:** Total 50 patients of age group >12 years, were included and studied thoroughly with regards to both history and clinical examination. Higher total leukocyte count (>13,700/mm<sup>3</sup>), serum creatinine (>2 mg/dl) and low serum albumin (<2.2 g/dl), and AF protein (<1.086 g/dl) were significantly associated with increased mortality. Reduction in polymorphonuclear leukocyte count in serial AF analysis showed reduction in mortality.

**Conclusion:** Increased total leukocyte count, low serum albumin, increased serum creatinine levels, and low AF protein are associated with poor prognosis. Serial AF cell count is helpful in predicting prognosis and can be used to monitor treatment.

**Key words:** Ascites, Ascitic fluid, Biopsy, Liver cirrhosis, Peritonitis, Prognosis

## INTRODUCTION

Cirrhosis of the liver is one of the commonly encountered liver disorders in a clinical practice caused by a wide variety of etiologies. It is defined anatomically as a diffuse process of

nodule formation and fibrosis in the liver. The pathological hallmark of cirrhosis is the development of scar tissue that replaces the normal parenchyma, blocking the portal flow of blood through the organ and disturbing the normal functions of the liver.<sup>1</sup> Patients with cirrhosis may have compensated liver disease and may manifest as anorexia, weight loss, weakness, fatigue, and even osteoporosis as a result of vitamin D malabsorption and subsequent calcium deficiency.<sup>2</sup> Decompensation of liver function may result in clinical symptoms such as jaundice, pruritus, gastrointestinal bleed, ascites, coagulopathy, and mental status changes and complications such as SBP, hepatic encephalopathy, and variceal bleeding from portal hypertension.<sup>2</sup>

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In most of the patients of cirrhosis terminal events are spontaneous bacterial peritonitis (SBP), hepatic encephalopathy, gastro intestinal bleeding, hepatorenal syndrome, hepatocellular carcinoma, and other infection due to decrease immunity.<sup>3</sup> Established cirrhosis has 10 years mortality rate between 34% and 66%.<sup>4</sup> The treatment is mainly directed against the prevention and management of the complications. Therefore, prompt and early diagnosis of these complications is the mainstay for prolonging life in cirrhotic patients. The SBP is a severe complication appearing in 8-22% of hepatic cirrhosis with ascites.<sup>5</sup>

### SBP

The SBP is by definition an infection of the previously sterile ascitic fluid (AF), without any apparent intra-abdominal source of infection. Polymorphonuclear (PMN) cell count of more than 250/mm<sup>3</sup> in AF is currently considered diagnostic of SBP and warrant the prompt start of antibiotic treatment.<sup>2</sup>

### AF Defense Mechanisms

The arrival of bacteria to the AF does not guarantee that infection will develop. In fact, cirrhotic AF is capable of humoral self-defense, mainly on the basis of the effectiveness of the complement system. Patients with adequate activity of this vital bactericidal system usually do not develop AF bacterial infections. However, it has been demonstrated that patients with low C3 component of complement in AF (<13 mg/dl) and/or a protein level of <1 g/dl, are predisposed to this infection. The complement levels may be deficient because of increased consumption of these components or because of impaired synthesis. Most of the bacteria that colonize AF are intestinal Gram-negative bacteria. The presence of lipopolysaccharides in their cell wall activates the alternative pathway of complement. If the complement levels are inadequate to effectively kill the bacteria, the infection will not develop.

### Predisposing factors for SBP<sup>6,7</sup>

1. Child-Pugh class C cirrhosis
2. AF protein level <1 g/dl or complement C3 level <13 mg/dl
3. Gastrointestinal bleeding
4. Urinary tract infection
5. Intestinal bacterial overgrowth
6. Iatrogenic causes- urinary bladder, intravascular catheters
7. Previous SBP.

The severity of the liver disease is probably the most important factor. Almost 70% of patients who develop SBP are Child-Pugh class C, with the remainder being

Class B.<sup>6</sup> A serum total bilirubin level of >2.5 mg/dl is an independent predictive factor of SBP. A direct correlation between total protein level, complement components, and opsonic activity explains why an AF total protein level of <1 g/dl is a risk factor for the development of infection.<sup>7</sup>

Alcohol consumption is rising all over the country, especially in the Northeastern part of India. Global information system on alcohol and health 2011 report shows high prevalence of alcohol consumption in this part of the country.

In Assam, 58% of the youth used at least one substance and 27.4% were concurrent users of both alcohol and tobacco.<sup>8</sup>

The survey, conducted by the Registrar General of India across 284 districts found that men from Chhattisgarh love their drink, recording the highest percentage prevalence at 31.6%, followed by Jharkhand (24.6%) and Assam (23.8%). When it comes to women, Assam ranked first. Around one in 10 adult women in Assam reported drinking alcohol followed by Jharkhand (8.2%), Chhattisgarh (7.4%) and Odisha (4.5%).<sup>9</sup>

The SBP is one of leading cause of death in decompensated liver disease which need prompt diagnosis and treatment. Studies have shown that causative bacteriological agent and empirical therapy guidelines are different in different part of world and even different in same region on different time periods.<sup>10,11</sup>

As this part of country has the increasing toll of alcoholic liver disease, the number of cirrhosis patients attending the Silchar Medical College and Hospital (SMCH) also has been increasing every year. SMCH is the only tertiary care center of Southern Assam having catchment area of whole Barak Valley, Manipur, Tripura, Mizoram, India. However, information regarding the clinical profile and bacteriological profile of SBP and its impact in cirrhotic patients is still lacking in many aspects in this part of country.

This study was undertaken with an idea to evaluate the significance of serial AF analysis and other biochemical markers to determine the prognosis in cirrhotic patients in this region.

### Study Design

Hospital-based, single centered, and observational study.

## MATERIALS AND METHODS

The present study was carried out on patients admitted to medicine ward, SMCH, Silchar, Assam. Patients admitted

for chronic liver disorder, and its complications were studied during the period from July 2013 to July 2014. Ultrasonography machine was used to diagnose cirrhosis of liver and ascites giving special reference to caudate lobe, portal vein, and spleen. All patients with hepatic cirrhosis, confirmed by ultrasound or liver biopsy, with ascites were included in the study.

SBP was diagnosed based on following criteria.

AF PMN leukocytes count >250 cells/mm<sup>3</sup>.

OR

AF total cells count >500 cells/mm<sup>3</sup> with >50% neutrophils.

AND

Absence of a primary source of infection.

About 50 patients of SBP were studied, diagnosed by above described guidelines, result of the present study are compared with other studies as follows.

Investigations such as complete blood count, serum protein and fraction, serum bilirubin, alanine transaminase, aspartate transaminase, fasting blood glucose, lactate dehydrogenase, AF analysis including culture sensitivity and acid-fast bacilli staining, hepatitis B surface antigen (HbsAg), anti-hepatitis C virus, prothrombin time/international normalized ratio were done.

**Serial AF Cell Count**

In patients suspected of SBP, ascitic tap was done before the therapy (day 0), 48 h and then every 5<sup>th</sup> day after starting antibiotic treatment until the final outcome of the disease. This was referred to as serial AF cell count. The fluid was analyzed for total protein, sugar, and the total and differential leukocyte count.

Intravenous cefotaxime 2 g every 8 h were used as treatment of SBP.

**RESULTS**

Total 50 patients of age group >12 years, diagnosed as SBP were studied thoroughly with regards to both history and clinical examination. The majority of patients (72%) were alcoholics while 12% were HBsAg positive. In 16% of patient’s etiology could not be determined and may be cryptogenic or nutritional (Tables 1 and 2).

Outcome was grave with 32% of mortality. Most of patients died due to SBP and hepatic-encephalopathy while some of the patients died due to hematemesis, hepatorenal syndrome and other complications of cirrhosis (Figure 1).

Mean total leukocyte count was above 13,700/mm<sup>3</sup> in 32% of cases. Higher total leukocyte count was significantly associated with increased mortality.

Mean serum creatinine levels were 1.05 in survived group while it was 2.0 in patients who expired. Elevation of creatinine >2 was associated with increased mortality and was a poor prognostic marker.

Mean AF protein level was 1.29 g/dl with the majority of patients survived. AF protein levels <1.086 g/dl is poor prognostic sign. Mean serum albumin is 2.212 g/dl in

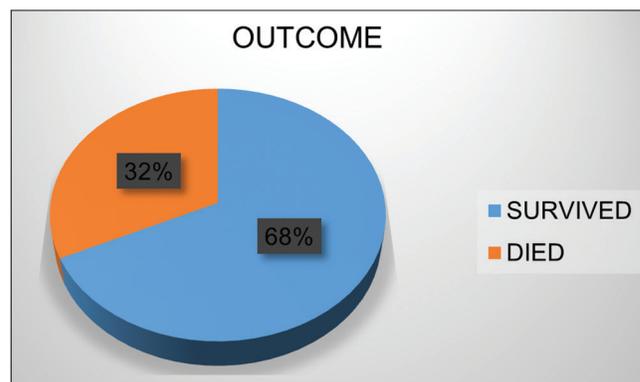
**Table 1: Symptom distribution in SBP patients**

Symptoms	N (%)
Abdominal distension	50 (100)
Abdominal pain	29 (58)
Fever	31 (62)
Jaundice	35 (70)
Altered sensorium	20 (40)
Hemetemesis/melena	17 (34)
Oliguria	20 (40)

SBP: Spontaneous bacterial peritonitis

**Table 2: Signs distribution of patients**

Sign	N (%)
Fever	31 (62)
Icterus	35 (70)
Asterixis	26 (52)
Hypotension	14 (28)
Abdominal tenderness	36 (72)
Ascites	50 (100)
Hepatomegaly	5 (10)
Splenomegaly	15 (30)



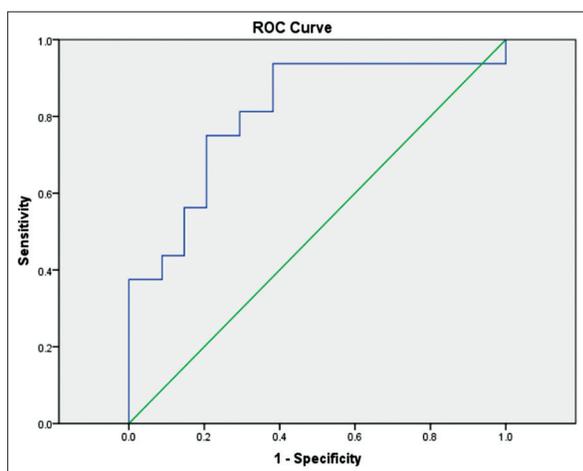
**Figure 1: Outcome in the present study**

survived while serum albumin <1.9 g/dl is poor prognostic sign (Table 3).

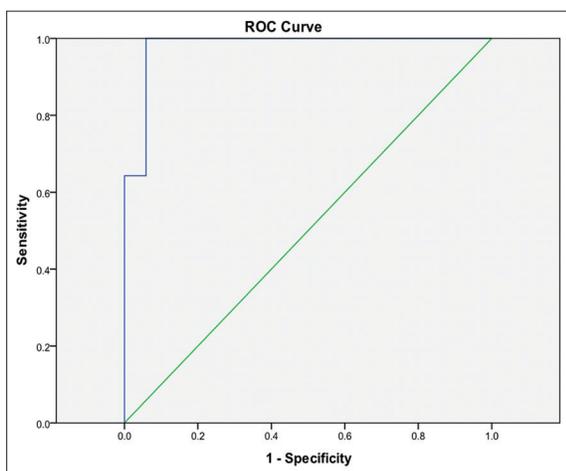
**Table 3: Comparison of investigations between the patients of SBP and those who died of it**

Investigations	Outcome				P value
	Survived		Died		
	Mean	SD	Mean	SD	
Total count	10168.32	5751.82	13765	5588.75	0.044*
Total bilirubin	4.75	3.61	6.32	4.29	0.2151
SGOT	145.61	112.69	202.75	195.64	0.145
SGPT	182.44	211.3	205.75	197.39	0.706
Serum albumin	2.212	0.43	1.9	0.37	0.0134*
Serum creatinine	1.05	0.28	2	1.5	0.0231*
AF protein	1.29	0.33	1.086	0.3	0.04337*

\*: Significant p value is < 0.05, SD: Standard deviation, SGOT: Serum glutamic oxaloacetic transaminase, SGPT: Serum glutamic pyruvic transaminase, AF: Ascitic fluid, SBP: Spontaneous bacterial peritonitis



**Figure 2: The receiver operating characteristics (ROC) for ascitic fluid cells at 0 h to predict the death, area under ROC curve: 0.809**



**Figure 3: The receiver operating characteristics (ROC) for ascitic fluid cells at 48 h to predict the death, area under ROC curve: 0.979**

**AF Cell Count at the Time of Diagnosis and Serial AF Cell Count (Tables 4-9 and Figures 2-4)**

Mean AF PMN cell count at the time of diagnosis was 492/mm<sup>3</sup> in patients of SBP who survived while it was 1721/mm<sup>3</sup> in patients who died. Thus, a high AF PMN count at the time of diagnosis was associated with poor prognosis.

AF PMN count of >600/mm<sup>3</sup> at time of diagnosis indicated poor prognosis with sensitivity of 87.5% and specificity of 78%.

**Table 4: Comparison of AF (PMN) cells count between the patients who died and survive**

Investigations	Outcome				P value
	Survived		Died		
	Mean	SD	Mean	SD	
AF cells (PMNs) 0 h	492.76	215.96	1721.68	1740.25	0.013*
AF cells (PMNs) 48 h	311	76.42	1235.75	1336.72	0.014*
AF cells (PMNs) 5 days	80.82	77.91	447.88	585.85	0.025*

PMN: Polymorphonuclear, AF: Ascitic fluid, SD: Standard deviation, \*=Significant p value is < 0.05

**Table 5: % change in AF cell count in 48 h of therapy between the patients who died and survived**

Investigations	Outcome (% change)	
	Survived	Died
AF cells (PMNs) 48 h	36.78	28.22
AF cells (PMNs) 5 days	83.60	65.97

PMN: Polymorphonuclear, AF: Ascitic fluid

**Table 6: Prediction of death based on AF cells (PMN) at 0 h**

AF cells at 0 h	Sensitivity (%)	Specificity	Accuracy	LR+	LR-
>450	100	61.76	74	2.54	0
>500	87.5	61.76	70.00	2.22	0.2
>550	87.5	67.64	74	2.62	0.18
>600	87.50	75.52	78.00	3.30	0.17
>650	81.20	79.41	80.00	3.94	0.23
>750	68.75	85.28	80	4.67	0.36
>800	65.25	88.23	78.00	4.80	0.49

PMN: Polymorphonuclear, AF: Ascitic fluid

**Table 7: Prediction of death based on AF cells (PMN) at 48 h**

AF cells at 48 h cut-off	Sensitivity (%)	Specificity (%)	Accuracy (%)
>200	87.50	3.00	30
>250	87.50	17.65	40
>300	87.50	52.94	44
>350	87.50	82.35	84
>450	87.50	94.15	88
>600	80.36	97.05	88

PMN: Polymorphonuclear, AF: Ascitic fluid

AF PMN count of  $>450/\text{mm}^3$  at 48 h predicted poor prognosis with sensitivity of 87.5% and 94.15%.

A fall in AF cell count from the time of diagnosis to, at 48 h was associated with good prognosis. Achievement of AF PMN cell count of  $<450/\text{mm}^3$  or  $>28\%$  reduction at 48 h of treatment was associated with good outcome.

In present study, the 5<sup>th</sup> day data shows that ascitic PMN cell count  $<200$  associated with good outcome.

### AF Culture and Sensitivity (Figure 5)

AF culture did not show any growth in 56% of cases while 38% showed *Escherichia coli*, 8% showed *Klebsiella*, and 2% showed of *Peptostreptococcus*, and 4% showed *Staphylococcus aureus*. \*\*8% patients had mixed flora in culture. Out of 22 cases which showed positive culture result, in 17 (77.27%) cases isolated organism showed sensitivity to cefotaxime (Figure 6).

Only 8% of patients had shown blood culture positive with 2% showing *Klebsiella*, 4% patients showing growth of *E. coli* and 2% *S. aureus*.

## DISCUSSION

About 50 patients of SBP was studied, diagnosed by above described guidelines, result of present study are compared with other studies as follows:

### Factors Predicting Mortality in SBP

Increased total leukocyte count, creatinine  $>2$  mg/dl and low serum albumin  $<2.2$  g/dl and low AF protein  $<1.086$  g/dl was significantly associated with increased mortality in the present study. Increased serum bilirubin

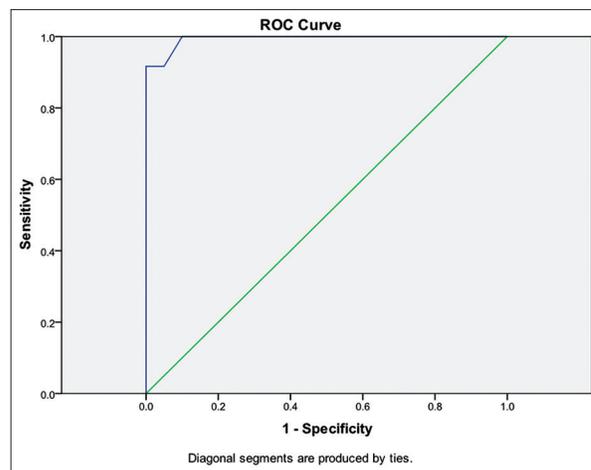


Figure 4: The receiver operating characteristics (ROC) for ascitic fluid cells at 5 days to predict the death, area under ROC curve: 0.994

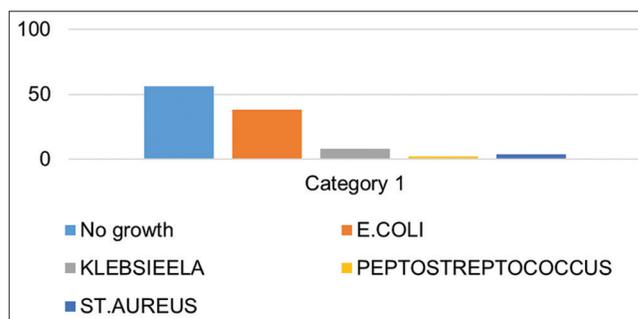


Figure 5: Ascitic fluid culture in present study

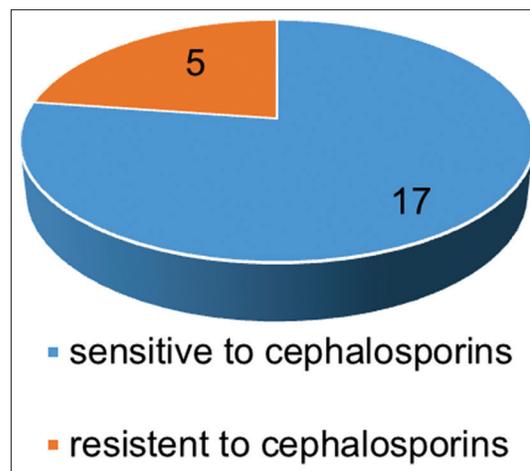


Figure 6: Sensitivity to cefotaxime to isolated organism

Table 8: Prediction of death based on AF cells at 5<sup>th</sup> day

AF cells at 5 <sup>th</sup> day cut off value	Sensitivity (%)	Specificity (%)	Accuracy (%)
>50	100	0	37.5
>100	100	20	50
>150	100	65	78.13
>200	100	85	90.63
>250	75	100	90.63

AF: Ascitic fluid

Table 9: Prediction of death based on AF cells (PMN)

AF cells	Cut-off	Sensitivity	Specificity	PPV	NPV	Accuracy	Area under ROC
AF cells (PMNs) 0 h	>600	87.5	73.52	59.09	89.28	78	0.809
AF cells (PMNs) 48 h	>450	87.5	94.15	87	94.11	88	0.979
AF cells (PMNs) 5 days	>200	100	85	80	100	93.63	0.994

PMN: Polymorphonuclear, AF: Ascitic fluid, NPV: Negative predicative value, PPV: Positive predicative value, ROC: Receiver operating characteristics

above 6.32 mg/dl was also associated with increased mortality, but it was not statistically significant.

Even studies by Filik *et al.*<sup>12</sup> and Rawat *et al.* showed association of increased total count, increased bilirubin levels and high creatinine levels with mortality.

According to study by Filik *et al.* decreased serum albumin and AF protein was related to mortality similar to the present study but in study by Rawat *et al.* fails to find any such correlation.

Sort *et al.*<sup>13</sup> 1999, Kamani *et al.*<sup>14</sup> 2008 also concluded that increased creatinine and low serum albumin is poor prognostic factor.

AF protein plays an important role in developing SBP in these patients. Patients with AF protein <1 g/dl are frequently predisposed to SBP. In Runyon *et al.*<sup>15</sup> series the patients with AF protein <1 g/dl were more predisposed to the development of SBP. In the series of Amarapurkar<sup>16</sup> the mean AF protein was 0.78 ± 0.24 g/dl in patients of SBP.

In the present series the mean AF protein was 1.086 ± 0.3 g/dl indicating the role of low AF in developing SBP.

Low AF protein was significantly related to mortality (Table 10).

**AF Biochemical Analysis (Table 11)**

**AF cell count**

In the present series, the AF cell count at the time of diagnosis, as well as that done at 48 hours was significantly related to outcome. A very high cell count at the time of diagnosis was associated with increased mortality. The AF cell count done at 48 h was also related significantly to outcome. The % fall in AF cell count from 0 h to 48 h was also related significantly to mortality (28% in the present study which is comparable to previous studies).

According to study by Rawat *et al.* the AF cell count at the time of diagnosis was not significantly related to mortality. This may have been due to less number of patients studied. While the AF count done at 48 h was significantly related to outcome. The attainment of AF cell count of < 250/mm<sup>3</sup> during the course of treatment was also associated with better outcome, which was consistent with the results of present study (Rawat, Bhatnagar<sup>17</sup>, Lady Harding College, New Delhi, Diamond APICON 2005). AF PMN count of >700/mm<sup>3</sup> at time of diagnosis and > 450/mm<sup>3</sup> at 48 h was associated with poor prognosis. A progressive fall in AF cell PMN count at 24, 48 h, and 5 days as compared to AF cell count at the time of diagnosis was associated with good prognosis. Achievement of AF PMN cells count

of <200/mm<sup>3</sup> at 5 days of treatment was associated with good outcome (Krishnamurthy and Patil 2008)<sup>18</sup>. These all results are comparable to the present study.

A fall of AF cell count <250/mm<sup>3</sup> can be used as a guide for duration of antibiotic therapy in treatment of SBP (Rawat *et al.*, Bhatnagar). In present study also patient who attained AF PMN cell count <200/mm<sup>3</sup> had good outcome. Hence, AF PMN<200/mm<sup>3</sup> can be used to guide the duration of therapy in SBP (Table 12).

**Summary**

1. Total leukocyte count >13,700/mm<sup>3</sup>, serum albumin <2.2 g/dl were associated with increased mortality and served as poor prognostic marker in SBP.
2. An AF PMN count >600/mm<sup>3</sup> at diagnosis, >450/mm<sup>3</sup> at 48 h of treatment and >250/mm<sup>3</sup> at the 5<sup>th</sup> day of treatment was associated with poor prognosis.
3. >28% reduction in AF cell PMN count after 48 h of treatment denoted successful antibiotic therapy and good prognosis.

**Table 10: Comparison in prognostic factor in SBP in different studies**

Study	Poor prognostic factors
Filik <i>et al.</i> , Rawat <i>et al.</i>	1. High bilirubin 2. High TLC 3. High creatinine
Sort <i>et al.</i> , Kamani <i>et al.</i>	1. High creatinine 2. Low serum albumin
Present study	1. High TLC 2. High bilirubin 3. High creatinine 4. Low serum albumin 5. Low AF protein
Agrawal <i>et al.</i>	1. Low AF protein

AF: Ascitic fluid, TLC: Thin-layer chromatography, SBP: Spontaneous bacterial peritonitis

**Table 11: Comparison of value of AF protein predisposing SBP**

Study	Runyon <i>et al.</i>	Amarapurkar <i>et al.</i>	Present study
Value of AF protein predisposing SBP (g/dl)	<1	<1	<1.08

SBP: Spontaneous bacterial peritonitis, AF: Ascitic fluid

**Table 12: Comparison of serial AF count (PMN) for poor prognosis in SBP studies**

Study PMN count	Rawat <i>et al.</i>	Krishnamurthy <i>et al.</i>	Present study
0 h	-	>700	>600
48 h	>250	>450	>450
Further analysis	>250	>200	>200

SBP: Spontaneous bacterial peritonitis, PMN: Polymorphonuclear, AF: Ascitic fluid

4. In the present series, the mean AF protein was 1.086 g/dl indicating low AF protein being the risk factor in developing SBP.

Drawback of the present study is small sample size. Further study, with big sample size will definitely give better guidance in these aspects.

## CONCLUSION

All patients of cirrhosis of the liver with ascites should be screened for SBP as no specific symptoms can define the SBP. As many patients may be asymptomatic. SBP carries a very high mortality and should be treated aggressively. Increased total leukocyte count, low serum albumin, increased creatinine levels and low AF protein is associated with poor prognosis. Once SBP is diagnosed, serial AF cell count is helpful in predicting prognosis and can be used to monitor treatment.

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# Ultrasound Evaluation of Vaginal Bleeding in First Trimester of Pregnancy: A Comparative Study with Clinical Examination

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## Abstract

**Introduction:** Vaginal bleeding in the first trimester is a common obstetric situation ranging from an insignificant episode to life threatening emergency. The major causes are abortion, ectopic, and molar pregnancy. Ultrasonography is playing an increasing role in the diagnostic process. This study was taken up to evaluate its utility vis-à-vis clinical examination findings.

**Methods:** This was a prospective study done at JSS Hospital Mysore, a tertiary care teaching hospital. All obstetric cases with a history of bleeding per vagina in the first trimester of pregnancy between November 2007 and September 2009 were included. A complete general physical and pelvic examination was done to arrive at a clinical diagnosis. Patients were then subjected to ultrasound examination. Clinical diagnosis and ultrasound diagnosis were correlated.

**Results:** 165 of all obstetric cases (4247) had the first trimester bleeding (incidence of 4%). Commonest causes were abortion (83%), ectopic (13%), and molar pregnancy (4%). Of 165 cases, 106 cases were correctly identified by ultrasonography. 59 cases proved by sonography were misdiagnosed by clinical examination with a disparity of 64%. 46 cases were diagnosed by ultrasonography as viable pregnancies with sensitivity, specificity negative predictive value (NPV), and positive predictive value (PPV) of 100% and 98 cases were diagnosed as non-viable pregnancies by ultrasonography with sensitivity of 98%, specificity of 100%, and NPV of 98%. The clinical diagnosis had sensitivity of 82%, specificity of 52%, and PPV of 40% in diagnosing viable pregnancies. In diagnosing non-viable pregnancies, clinical diagnosis had a very poor statistical correlation with sensitivity of 50%, specificity of 81%, PPV of 62%, and NPV of 72%.

**Conclusion:** This study reinforces results of earlier reports that ultrasound is a sensitive and specific non-invasive diagnostic tool in the evaluation of first trimester bleeding.

**Key words:** Abortion, Ectopic pregnancy, First trimester bleeding, Molar pregnancy, Ultrasonography

## INTRODUCTION

Vaginal bleeding in the first trimester is frequently encountered situation causing anxiety to the patient and obstetrician alike. 20-25% of pregnant women will have bleeding during early gestation.<sup>1</sup> This may range from

an insignificant episode to life threatening emergency.<sup>2</sup> The major causes are abortion, ectopic pregnancy, and molar pregnancy. Before the advent of ultrasonography (USG), these patients were managed only clinically.<sup>3</sup> Ultrasonography has revolutionized the management of early pregnancy complications.

The social phenomena of increasing maternal age and heightened expectations for a normal outcome have put increased pressure on the obstetrician, thereby leading to increased use of ultrasonography. This study was taken up to compare the utility of ultrasound vis-à-vis clinical examination findings in first trimester vaginal bleeding.

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## METHODS

This was a hospital-based prospective study. The study included patients attending JSS Hospital with a history of bleeding per vaginam in the first trimester of pregnancy. The study period was 2-year between November 2007 and September 2009. Women having non-obstetric causes for vaginal bleeding in the first trimester of pregnancy were excluded. The study was cleared by the Institutional Ethical Committee of JSS Medical College.

Clinical data such as age, parity, obstetric history, personal history, menstrual history, and details of present pregnancy such as period of amenorrhea at the time of first episode of bleeding, amount and duration of bleeding, pain abdomen and history of expulsion of fleshy mass/clots were noted. A detailed general physical and pelvic examination was done to arrive at a provisional clinical diagnosis. All patients were subjected to transabdominal sonography. Ultrasonography was done using Siemens Sonoline G608 and Toshiba Nemio machines. Transvaginal sonography (TVS) was performed whenever transabdominal sonography was inconclusive or equivocal. Transabdominal sonography was done and TVS using 5-7 MHz transducer. The clinical examination findings and operative procedures were noted. Clinical and ultrasound findings were correlated. A  $P < 0.05$  was used to assess for statistical significance.

### Statistical Analysis

The descriptive procedure was used to display univariate summary statistics for several variables in a single table. The frequencies procedure was used for describing many types of variables. The Crosstabs procedure was used to measure of association for two-way tables. The Chi-square test procedure was used to tabulate variables into categories. All the statistical methods were carried out through the SPSS for Windows (version 16.0).

## RESULTS

The total number of obstetric admissions was 4247, out of which 165 had bleeding per vagina in the first trimester constituting a percentage of 4%. The age ranged from 16 to 35 years. The majority were in the age group of 21-25 years (46%). 45 (29%) were in the age group 16-20 years, 38 (22%) in the age group 26-30 years, and 7 (4%) between 31 and 35 years (Table 1). 87 (53%) cases were primigravida, and 78 (47%) were multigravida. The difference was not statistically significant. The mean gestational age at which cases presented with bleeding in the first trimester was 9 weeks. The majority of the cases, 57 (35%) with bleeding per vaginam were between gestational age 6.1 and 8 weeks. 53 (32%) had bleeding at 8.1-10 weeks and 55 (33%) at age

10.1-12 weeks. The difference in the gestational age was not statistically significant. 110 cases (66.7%) had uterine size  $< 10$  weeks and 55 (33.3%) had uterine size between 10 and 12 weeks. Cervical Os was open in 23 (14%) and closed at 142 (86%). Fornices were free in 160 (97%), and forniceal tenderness was present in 5 cases (3%) (Table 2). 94 out of 165 (57%) cases were clinically diagnosed as threatened abortion. 52 (31%) were diagnosed clinically as incomplete abortion and 7 (4%) as missed abortion, 9 (6%) of 165 cases were diagnosed as ectopic pregnancy and 2 (1.2%) as molar pregnancy. 1 (0.8%) as complete abortion. The distribution of cases according to clinical diagnosis was statistically significant ( $P = 0.000$ ) (Table 3). On sonography of 165 cases, 46 showed signs of viable pregnancy, 41 (24%) showed incomplete abortion, in 28 (17%) missed abortion, in 18 (11%) anembryonic gestation, in 21 (13%) ectopic pregnancy, 5 (3%) complete abortion, and 6 (4%) were diagnosed as molar pregnancy. The difference in the ultrasonographic features were statistically significant ( $P = 0.000$ ) (Table 4).

Out of 165 cases, 46 (12%) were diagnosed as threatened abortion, 41 (11%) as incomplete abortion, 28 (25%)

**Table 1: Representing distribution of cases according to age group**

Age in years	N (%)	
16-20	45 (27)	Mean±SD: 23.4±3.8163
21-25	75 (46)	Chi-square: 56.648
26-30	38 (23)	df: 3
31-35	7 (4)	$P=0.000$
Total	165 (100)	

SD: Standard deviation

**Table 2: The causes of bleeding per vaginam in the first trimester of pregnancy**

Causes	N (%)	
Abortion	138 (83)	Chi-square: 189.9
Ectopic pregnancy	21 (13)	df: 2
Hydatidiform mole	6 (4)	$P=0.000$
Total	165 (100)	

**Table 3: Disparity between clinical diagnosis and ultrasound diagnosis**

Cases	Clinical diagnosis	Ultrasound diagnosis	Disparity
Threatened abortion	94	46	48
Incomplete abortion	52	41	11
Complete abortion	1	5	4
Missed abortion	7	28	21
Anembryonic gestation	-	18	18
Ectopic pregnancy	9	21	12
Molar pregnancy	2	6	4
Total	165	165	118

as missed abortion, 5 (3%) as complete, 18 (17%) as anembryonic, 21 (28%) as ectopic, and 6 (4%) as molar pregnancy. The difference in the number of cases was statistically significant ( $P = 0.000$ ).

Out of 165 cases, 138 (83%) had the abortion as the major cause of bleeding. The second common cause was ectopic pregnancy constituting (13%) followed by hydatidiform mole (4%). Out of 94 cases of threatened abortion diagnosed clinically, only 46 cases were sonographically confirmed as threatened abortion. There was disparity in 48 cases of threatened abortion which without the aid of ultrasonography would not have received appropriate treatment. The disparity in case of incomplete abortion was 11 and in missed abortion was 21. The disparity in cases of ectopic was 12, in cases of complete abortion was 4, and in case of molar pregnancy disparity was 4. The total disparity between clinical diagnosis and ultrasound diagnosis was present in 118 cases (71%) (Table 5).

Out of 165 cases, clinical diagnosis was confirmed by sonography in 106 indicating accuracy of clinical diagnosis to be 64%. In the follow-up of clinically diagnosed cases, out of 94 cases of suspected threatened abortion, 38 cases were confirmed by sonography out of which 32 cases continued to term gestation. 14 cases of incomplete abortion were misdiagnosed as threatened abortion. 15 cases of missed abortion, 14 cases of anembryonic gestation, 3 cases of complete abortion, 7 cases ectopic, and 3 cases of molar pregnancy were misdiagnosed as threatened abortion. Out of 52 cases of incomplete

abortion diagnosed clinically, only 27 were confirmed. 6 cases of missed abortion and 8 cases of threatened abortion were misdiagnosed as incomplete abortion. 4 cases of anembryonic gestation, 1 case of complete abortion, 5 cases of ectopic pregnancy, and 1 case of molar pregnancy were misdiagnosed as incomplete abortion. Out of 7 cases of missed abortion diagnosed clinically, all 7 cases are confirmed. 1 case of complete abortion, 9 cases of ectopic pregnancy, and 2 cases of molar pregnancy diagnosed on clinical examination were confirmed.

Out of 46 cases, which were diagnosed as threatened abortion on ultrasound, 32 cases were continued as a normal pregnancy, 8 had missed abortion, 2 had incomplete abortion, and 4 had complete abortion. All other causes of bleeding per vagina were confirmed on ultrasound.

The subjects in the study group were divided into three main categories for the purpose of statistical correlation: (1) Viable intrauterine pregnancy, (2) Non-viable intrauterine pregnancy, and (3) Ectopic pregnancy. All cases of viable intrauterine pregnancies were followed up without intervention while other cases were managed appropriately based on the ultrasound findings. 46 out of 94 cases of suspected viable intrauterine gestation on clinical examination were confirmed. This shows sensitivity of 82%, specificity of 52%, PPV of 40%, and NPV of 88%. Of the 9 ectopic pregnancies diagnosed clinically, all were confirmed with specificity of 100%, PPV of 100%, and NPV of 92%. In diagnosing non-viable pregnancies, the clinical diagnosis had a very poor statistical correlation with sensitivity of 50%, specificity of 81%, PPV of 62%, and NPV 72% (Table 6).

Extrauterine pregnancies were correctly diagnosed on ultrasound with zero false positive and zero false negativity with sensitivity, specificity, PPV, and NPV of 100% each. All ectopic pregnancies were correctly diagnosed with sensitivity of 100%, specificity of 99%, PPV of 95%, and NPV of 100%. One case which was diagnosed as ruptured ectopic was found to be unruptured ectopic on laparotomy. The non-viable pregnancies diagnosed on ultrasound were confirmed with a sensitivity of 98% and NPV of 98%. Ultrasound diagnosis proved to be very accurate on statistical evaluation of sensitivity and specificity of 100% (Table 7).

**Table 4: Comparison of clinical, ultrasound, and final diagnosis**

Parameters	N (%)		
	Clinical diagnosis	Ultrasound diagnosis	Final
Threatened abortion	94 (57)	46 (12)	46 (12)
Incomplete abortion	52 (31)	41 (11)	41 (11)
Missed abortion	7 (4)	28 (25)	28 (25)
Complete abortion	1 (1)	5 (3)	5 (3)
Anembryonic gestation	-	18 (17)	18 (17)
Ectopic pregnancy	9 (6)	21 (28)	21 (28)
Molar pregnancy	2 (1)	6 (4)	6 (4)
Total	165 (100)	165 (100)	165 (100)

**Table 5: Correlation of clinical diagnosis with final diagnosis - an evaluation**

Parameters	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Viable	82	52	40	88
Ectopic	40	100	100	92
Non-viable	50	81	62	72

PPV: Positive predictive value, NPV: Negative predictive value

## DISCUSSION

Bleeding in early pregnancy is an indicator of an abnormality interrupting the normal development. It is a common cause for emergency admissions. If a diagnosis of the viability or non-viability of pregnancy can be made definitely then, hormonal therapy and hospitalization can

**Table 6: Correlation of ultrasound diagnosis with final diagnosis - observation**

Parameters	True positive	False positive	False negative	True negative
Viable	46	0	0	119
Ectopic	20	1	0	144
Non-viable	98	0	1	67

**Table 7: Correlation of ultrasound diagnosis with final diagnosis - an evaluation**

Parameters	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Viable	100	100	100	100
Ectopic	100	99	95	100
Non-viable	98	100	100	98

PPV: Positive predictive value, NPV: Negative predictive value

be avoided.<sup>4</sup> By clinical history and examination, this is usually impossible. The availability of ultrasonography has changed the scenario.<sup>5</sup>

The incidence of bleeding in the present study was 4%. 35% of patients in this study had bleeding at 6-8 weeks of gestation which is comparable to the study by Bharadwaj *et al.*<sup>6</sup> of 30%. 32% of cases had bleeding at 8.1-10 weeks and 33% at between 10 and 12 weeks compared to 35% and 22%, respectively, in the Bharadwaj study.<sup>6</sup>

In the present study, abortions contributed to a major cause of the first trimester bleeding constituting 83%. In the reports by Rani *et al.*<sup>7</sup> and Bhargava *et al.*, also abortion was the leading cause with an incidence of 61% and 81.6%, respectively. The incidence of ectopic pregnancy was 13% which is similar to that reported by Bhargava *et al.* The incidence of mole in present study was 4% compared to the studies of Rani *et al.* and Bhargava *et al.* who reported an incidence of 18% and 4.35%, respectively.

In our study, out of 46 cases of sonographically diagnosed threatened abortion, subchorionic bleed was noted in 33 cases which constitutes 71%, when compared to Steven *et al.*<sup>8</sup> 10 (20%) and Pederson *et al.*<sup>9</sup> 62 (18%). We noted an increased incidence of subchorionic bleeds in our study.

In this study, the incidence of viable pregnancies on ultrasound was 27% and 72 % of non-viable pregnancies which is similar to the study by Schauburger *et al.*<sup>5</sup> and Stabile *et al.*<sup>10</sup> had an incidence of 58%, 44%, and 64% of viable pregnancies and 42%, 52%, 36% of non-viable pregnancies, respectively.

In this study, 106 clinically diagnosed cases were confirmed on ultrasound with the disparity of 64%. The present study is comparable to the study by Ghorade *et al.*,<sup>11</sup> whereas

Khanna<sup>12</sup> and Reddi Rani noted a disparity of 50% and 42% between clinical and ultrasound diagnosis, respectively. In this study, all cases of threatened abortion, missed abortion, incomplete abortion, complete abortion, anembryonic gestation, and molar pregnancy were diagnosed accurately on ultrasound with an accuracy of 100%. The results of our study are comparable with that of Sofat<sup>13</sup> and Bharadwaj.<sup>6</sup> Lower incidence of blighted ovum was noted in the study of Gorade *et al.*<sup>11</sup> This could be because cases of up to 20<sup>th</sup> week of gestation had been taken up in their study (incidence of blighted ovum decreases with the advancing gestational age).

Rajan<sup>14</sup> in a prospective study of 140 patients observed that there were 37 (26.43%) subjects with vaginal bleeding, which was observed at or before 8 weeks in 91.89%. Pregnancy was normal by sonography, based on the imaging of live fetus, in 20 (54.05%). The abnormal pregnancies diagnosed included blighted ovum (18.92%), vesicular mole (16.22%), missed abortion (11.76%), and ectopic pregnancy in (11.76%). This study highlighted the invaluable role of sonography in investigating early pregnancy bleeding, wherein a normal pregnancy with excellent chances for viable births could be differentiated from a pathological pregnancy which warrants an immediate termination.

Sofat<sup>13</sup> compared and correlated clinical diagnosis and ultrasound diagnosis. They found that ultrasound had a definite edge over clinical diagnosis by about 30% in case of threatened abortion, 40% in missed abortion, 95% in molar pregnancy, and 35% in incomplete abortion.

Lyer and Bhattacharya<sup>15</sup> in their evaluation of 200 patients of complicated first trimester clinically and by ultrasonography found that of the 74 patients clinically diagnosed as threatened abortions, only 36 showed supporting ultrasonographic findings. USG was diagnostic of non-viable pregnancy in 34. 8 of the 40 patients suspected to have a missed abortion were- actually diagnosed as normal viable pregnancies, and 2 cases had an empty non-pregnant uterus. In 2 clinically diagnosed as complete abortion, significant products of conception were seen on USG. 12 of the 18 cases suspected of having a delayed period turned out to be either missed abortion or incomplete abortion. 6 of the 12 cases with suspected vesicular mole, 6 patients suspected of ectopic pregnancy, and two fibroid uterus were diagnosed on USG as having normal viable pregnancies. Judicious use of ultrasonography was advocated in the management of early pregnancy complications.

Jaideep Maihotra<sup>16</sup> in his prospective evaluation of 150 patients with first trimester bleeding found that ultrasonography helped in establishing the correct diagnosis in 32% of clinically misdiagnosed cases. He concluded that

ultrasonography was the only imaging modality, by which an accurate assessment of first trimester bleeding can be done from the diagnostic and prognostic point of view.

Reddi Rami<sup>17</sup> evaluated 100 cases of first trimester bleeding by ultrasonography. Abortion constituted the largest group (61%) followed by ectopic pregnancy (21%), and vesicular mole (18%). Sonography was strongly suggestive of ectopic in 72% and diagnostic in 23% of cases. TVS was diagnostic in 39% of cases. TVS was more sensitive than transabdominal sonography in the diagnosis of abnormal intra uterine gestation normal intrauterine gestation and ectopic pregnancy.

We agree that the sample size of this study could have been larger for better results. Furthermore, patients presenting with excessive vaginal bleeding undergoing immediate evacuation and curettage were excluded in this study, and this could have altered the results.

To summarize, in this study, the causes of bleeding covered a spectrum of conditions ranging from a viable pregnancy to non-viable pregnancy. Ultrasound examination was a good indicator for evacuation in cases of abortion. Using ultrasound, pregnancy with higher chances of a viable birth could be differentiated from a pathological pregnancy warranting an immediate termination.

The earlier concept was that nothing is better than the two fingers of an obstetrician, but today ultrasound has been shown to have a definite edge. Ultrasound is aptly described as the third finger of the obstetrician.

## CONCLUSIONS

Ultrasound is a valuable tool in the differentiation of causes of first trimester vaginal bleeding. Ultrasound is helpful in the decision-making algorithm about the safe continuation of the pregnancy, timely intervention for abnormal pregnancy. Judicious utilization of ultrasonography and a close liaison with the sonologist is necessary. However, it should be remembered that ultrasound is an extension of the pelvic examination and cannot replace obstetric history and clinical examination.

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# Screening for Asymptomatic Renal Disease among School Children from Chennai City, India

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## Abstract

**Background:** Urinary screening tests are vital for premature detection of renal diseases in asymptomatic school children and adolescents.

**Objectives:** The purpose of the study was to identify school children aged from 6 to 18 years with asymptomatic renal disease by urinalysis.

**Materials and Methods:** Two schools were selected from Chennai city and children between the ages 6 and 18 years attending these schools were included in the study. Children with past history of any renal or medical illness, acute febrile illness, and children with congenital malformations were excluded from the study.

**Results:** A total of 1000 school children between the ages of 6 and 18 years were screened for asymptomatic renal disease by performing urinalysis. A significant number (10.9%) of school children were positive for asymptomatic renal disease. Males constituted 55.6% of the total participants. Hypertension either systolic or diastolic was observed among 0.3% of participants. The prevalence of proteinuria, pyuria, and hematuria was found to be 4.3%, 5.2%, and 2.5%, respectively. The urinary abnormality was significantly more common in males (14.7%) compared to females (6.1%).

**Conclusions:** Urinary screening plays a pivotal role in the identification of occult renal diseases in asymptomatic children. Urinary screening is, therefore, useful in early detection and also provides a structural work up for a further plan that may lead to prevention, diagnosis, and management of renal diseases.

**Key words:** Asymptomatic, Children, Hematuria, Hypertension, Proteinuria, Pyuria, Urinalysis

## INTRODUCTION

Chronic renal disease in children has received little medical attention. This condition may be too overt for early detection. Mass urine screening tests in school are the simplest and least expensive way to detect urinary abnormalities which may suggest the presence of a chronic renal disease. A major question for renal medicine in developing countries is how to define strategies that can identify early enough those subjects who are

at risk of developing a renal disease in later life. Most epidemiological data on kidney disease originates from data available on end stage renal disease; little information is available on the prevalence of kidney disease. The epidemiological studies that have been performed provide evidence that end stage renal disease represents the tip of the iceberg.<sup>1</sup>

The incidence of end stage renal disease in children ranges from 5 to 6 per million children under the age of 15 years in Europe, Australia, and Japan, to 10 to 11 per million children in the United States of America.<sup>2</sup> The prevalence and incidence of renal disease in developing countries are not well known.<sup>3,4</sup> This lack of knowledge is an obstacle to the adoption of preventive measures which may be of great value in a social and economic environment where treatment of end stage renal disease are not available to the vast majority of population. Hence, screening of

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healthy children is useful in the detection of various kidney diseases.

The goal of a screening program is to recognize a disease in its preclinical phase so that intervention is possible.<sup>5</sup> For screening to be beneficial, it should fulfill certain criteria.<sup>6</sup>

The simplest and least expensive way of screening the apparently healthy subject is urinalysis.<sup>7,8</sup> Several studies have been made using reagent strips documenting their effectiveness in detecting urinary abnormalities at a relatively low cost. Mass screening helps to design population-oriented preventive measures that will limit the need for dialysis and transplantation. Prevention is more important in our setting given the shortage of financial resources and the fact that dialysis centers, equipment, and trained personnel are simply not available to the general population. Hence, this study was planned.

#### Aim of the Study

To identify School Children aged from 6 to 18 years with asymptomatic renal disease.

### MATERIALS AND METHODS

Children between the ages 6 and 18 years attending schools in Chennai city during the period June 2007-August 2008 were included in the study. Children with past history of any renal or medical illness, acute febrile illness, and children with congenital malformations were excluded from the study.

Two schools were selected for conducting the study. One was from a semi-urban location (Iyyapanthangal, Chennai, Government school) and other from an urban location (Shenoy Nagar, Chennai, Government School). A school health program was organized in each of these schools for 7-10 days, respectively. After obtaining informed consent from parents and teachers, students, who met inclusion and exclusion criteria, were selected for the study. A thorough physical examination was done including recording of weight, height, and Blood pressure (BP). Aseptic precaution was explained to the participants for collection of urine sample, and then midstream urine was collected in a clean plastic container. Urine was examined by dipstick for color, turbidity, pH, specific gravity, albumin, and glucose. After centrifugation 3000 rpm/min for 5 min sample was examined microscopically for red blood cell (RBC), white blood cell, casts, and bacteria. Students and school authorities were informed about abnormal urinary findings and were advised follow-up in the hospital for further evaluation. Children whose

urine examination showed any one of the following were considered to have urinary abnormality suggestive of a renal disease. Albumin  $\geq 2+$ , pus cells  $\geq 5$  cells/hpf, and RBC  $\geq 5$  cells/hpf. The study population was divided into two groups, one with urinary abnormality and the other without. These two groups were compared using the statistical methods. Data collected was analyzed using the statistical methods such as Chi-square test and Students *t*-test.

### RESULTS

A total of 1000 students, who fulfilled the inclusion and exclusion criteria between the ages 6 and 18 years were enrolled in the study. Students <10 years constituted 35.3%, while only 7.3% were between 17 and 18 years of age (Figure 1); this is because the less number of students were enrolled in the higher secondary classes. Among 1000 students screened 55.6% were males, and 44.4% were females (Figure 2). The age versus sex distribution shown in Figure 3 reveals more males compared to females in the age groups >12 years. Male students constituted 20.6% compared to 6.6% females in the age group 13-14 years. Parameters like distribution of age/sex versus weight and height centiles does not achieve any significance. In our study, 2 children had systolic BP of above 95<sup>th</sup> centile and they belonged to the age group of 13-14 years and the child with diastolic hypertension was in the age group of 11-12 years (Figures 4 and 5). Three samples

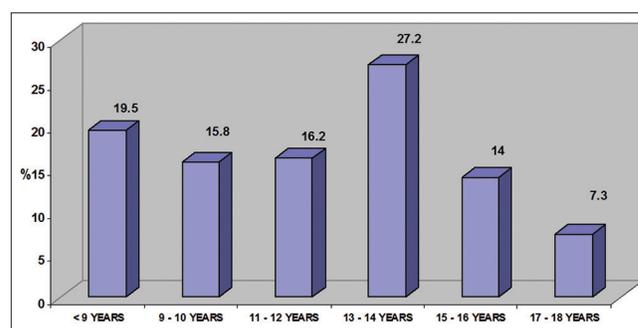


Figure 1: Age distribution

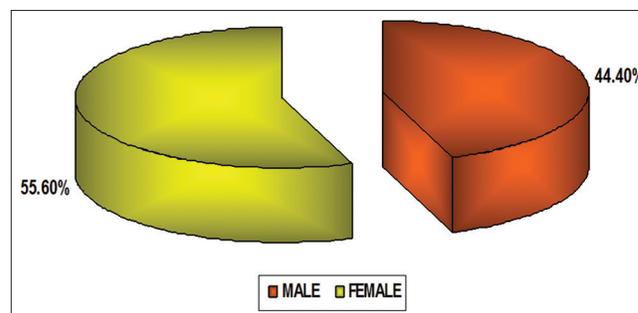


Figure 2: Sex distribution

were positive (0.3%) for glycosuria and 4.3% of children showed significant proteinuria (urine albumin  $\geq 2+$ ,  $P = 0.00$ ), which is significantly seen in males compared to females (Table 1). Pyuria and hematuria were detected in 5.2% ( $P = 0.00$ ) and 2.5% ( $P = 0.00$ ) of children, respectively, with significant male predominance (Tables 2 and 3). The participants were then divided into two groups, one group having any one of the above mentioned urinary abnormalities and the other group without any abnormalities. In our study, among 1000 participants, 10.9% (109) met the criteria for urinary abnormality and the percentage of children with urinary abnormalities increased as age progressed ( $P = 0.00$ , Figure 6). Urine abnormalities were more prevalent and significant in males compared to females ( $P = 0.00$ , Figure 7). Urine abnormalities were detected in all 3 children with

hypertension and were significant (Table 4). There was no significance attained between weight ( $<3^{rd}$ ) and height ( $<3^{rd}$ ) centiles against urinary abnormalities. Among the 52 children who had pyuria, 75% (39) of these children had isolated pyuria without significant proteinuria or hematuria, and these children, could be cases of urinary tract infection and the remaining 70 children with one or more urinary abnormality, could be cases of asymptomatic renal disease, who need further work up and follow-up to prevent progression to chronic renal failure.

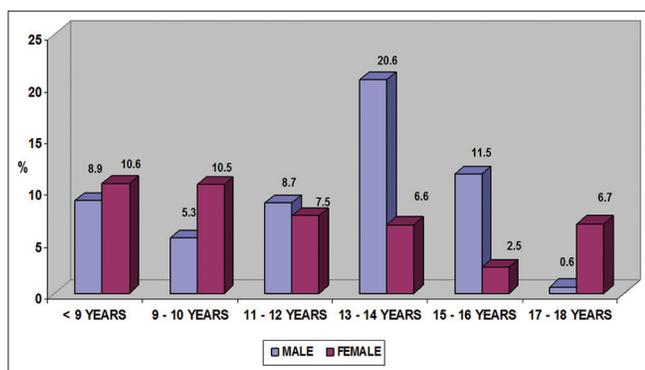


Figure 3: Age and sex distribution

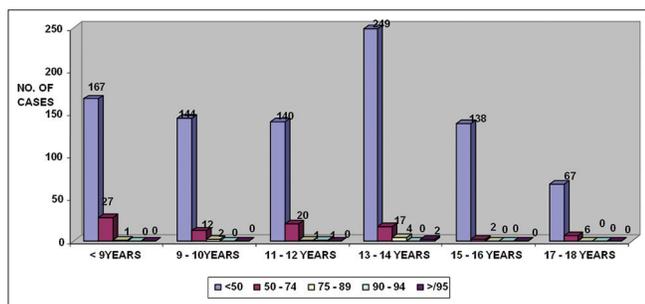


Figure 4: Age group and systolic blood pressure

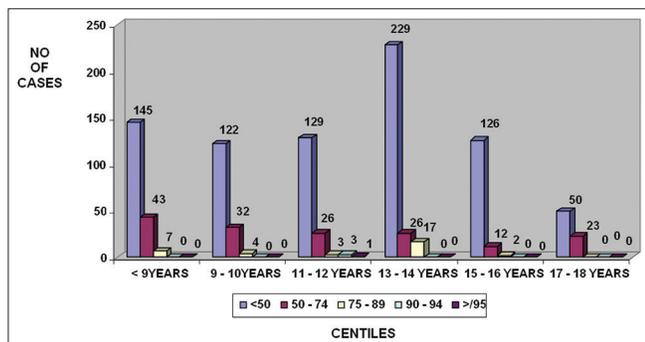


Figure 5: Age group and diastolic blood pressure

Table 1: Urinary albumin according to sex

Albumin/sex	n (%)		
	Female	Male	Total
Nil	422 (95)	477 (85.8)	899 (89.9)
Trace	7 (1.6)	17 (3.1)	24 (2.4)
1+	2 (0.5)	32 (5.8)	34 (3.4)
2+	11 (2.5)	27 (4.9)	38 (3.8)
3+	2 (0.5)	3 (0.5)	5 (0.5)
Total	444 (100)	556 (100)	1000 (100)

Table 2: Urinary pus cells according to sex

Pus cells/sex	n (%)		
	Female	Male	Total
Nil	1 (0.2)	1 (0.2)	2 (0.2)
Occasional	135 (30.4)	63 (11.3)	198 (19.8)
1-2	281 (63.3)	341 (61.5)	623 (62.3)
3-4	16 (3.6)	109 (19.6)	125 (12.5)
>5	11 (2.5)	41 (7.4)	52 (5.2)
Total	444 (100)	556 (100)	1000 (1000)

Table 3: Urinary RBC according to sex

RBC/sex	n (%)		
	Female	Male	Total
Nil	376 (84.7)	228 (41)	604 (60.4)
Occasional	8 (1.8)	48 (8.6)	56 (5.6)
1-2	49 (11)	237 (42.6)	286 (28.6)
3-4	5 (1.1)	24 (4.3)	29 (2.9)
>5	6 (1.4)	19 (3.4)	25 (2.5)
Total	444 (100)	556 (100)	1000 (100)

RBC: Red blood cell

Table 4: Relationship of BP and urinary abnormality

BP centile	n (%)			
	Systolic BP		Diastolic BP	
	Present	Absent	Present	Absent
<90	107 (10.7)	890 (89.3)	108 (10.8)	888 (89.2)
90-94	0 (0)	1 (100)	0 (0)	3 (100)
$\geq 95$	2 (100)	0 (0)	1 (100)	0 (0)
Total	109	891	109	891
P value	0.000		0.014	

BP: Blood pressure

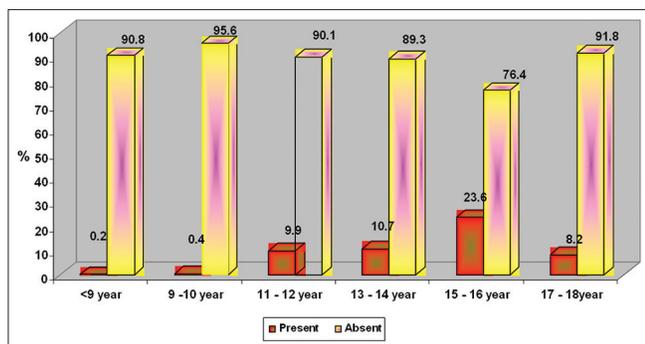


Figure 6: Age distribution and urine abnormality

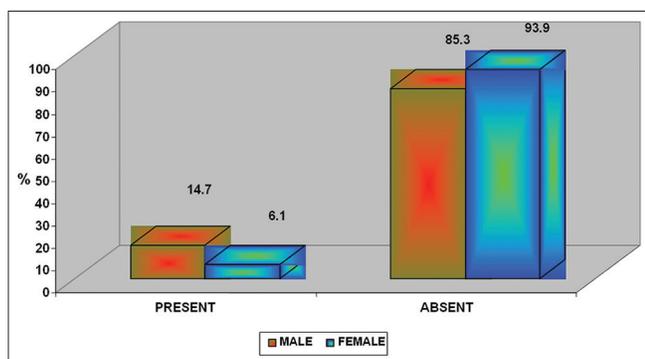


Figure 7: Sex distribution and urine abnormality

## DISCUSSION

Urinary screening test has been used to identify asymptomatic renal disease in children progressing to chronic kidney disease. Dipstick urinalysis is the most common test used for detecting urinary abnormalities in these children. In Asia, Japan was the first country to start a national urinary screening program for school children aged 6-14 years on an annual basis in 1973<sup>9</sup> Taiwan initiated a national program in 1990<sup>10</sup> covering children from 6 to 15 years old, while Korea's program began in 1998 for children from 6 to 18 years.<sup>11</sup> The process of screening was similar in all the studies. Urine collected from the children was tested using urine dipstick. Those children with proteinuria and/or hematuria underwent a second urinary screen. Those with persistent abnormalities were then referred to a pediatrician or nephrologist for further investigations. There is no such urinary screening program available in India. In our study, we did not do the second screening for children being tested positive in the initial screening.

Hypertension and proteinuria are the factors that contributed to progressive renal deterioration in children with chronic kidney disease, as validated by several studies.<sup>12-14</sup> The primary reduction in nephrons leads to secondary damage of the remaining nephrons due to the consequences of adaptive increases in glomerular

pressure and flow. Glomerular capillary hypertension is normally associated with enhanced transglomerular protein overload. Therefore, early detection of chronic kidney disease, with appropriate management of the risk factors for progression, may slow the development of end-stage renal failure in children.

In our study, the prevalence of urinary abnormalities was 10.9% (109) among the 1000 children subjected for urinary screening. This high prevalence may be explained by the fact that only a single urine sample was screened. This prevalence may be considerably lesser if repeat screening was undertaken. A lower prevalence rate of 0.12%-3.56% was reported by studies from Egypt,<sup>15</sup> Iran,<sup>16</sup> Malaysia,<sup>17</sup> and Japan<sup>9</sup> and all these studies initially had little higher prevalence and dropped to these range on further evaluation. In contrast, a higher prevalence (9.6-30.3%) has been reported in the first urinary screening by authors<sup>18-20</sup> from different geographic regions of the world. Variation in the detection rate of urinary abnormalities on screening in these studies may be due to varying ethnic backgrounds and the prevalence of renal diseases in these populations.

In our study, the prevalence of urinary abnormalities was significantly higher in the older age group, and this was in concordance with other studies.<sup>21-23</sup> In the current study, the male to female ratio was 14.7:6.1 in detection of urinary abnormalities. Lin *et al.*<sup>10</sup> found abnormalities in more males than females, whereas other authors demonstrated urinary abnormalities to be more common in females.<sup>24,25</sup> However, Vehaskari and Rapola.<sup>26</sup> found that the prevalence of abnormalities was not age or gender dependent.

Proteinuria was found in 4.3% of children, and significant proteinuria (urine albumin >2+) is more common seen in boys who are in concordance with Aladekoma *et al.*<sup>4</sup> Hematuria was seen in 2.5% of children with significant male predominance. Several studies demonstrated increased prevalence of hematuria as the age of the study population increased.<sup>3,27</sup> Carel *et al.* found hematuria to be more common in females than males in his urine screening of adult population while Hanif *et al.*<sup>28</sup> found there is no significant difference between two sex in the prevalence of hematuria. 5.2% children had significant pyuria with male preponderance in accordance with studies done by Hanif *et al.*<sup>28</sup> and Plata *et al.*<sup>18</sup>

In the current study, the prevalence of hypertension was found to be 0.3% (>95<sup>th</sup> centile) which includes both systolic and diastolic BP. This finding was similar to the study conducted by Anand and Tandon.<sup>29</sup> All the 3 children, who had hypertension, were in the age group of 11-14 years and they also had urinary abnormality, which indicates that these children were suffering from some renal disease.

Urine screening in school children is a non-invasive and viable test for early detection of silent renal diseases. Until now, there is no clear consensus statement about urinary screening program to be done for children and adolescent with asymptomatic renal disease in developing countries. Mass urinary screening programs are well recognized in some Asian countries (Japan, Korea, and Taiwan), but this is not the case for North America and Europe because of concern about cost-effectiveness. Sekhar *et al.* analyzed the cost-effectiveness of urinary screening programs, found them to be an ineffective procedure for primary care providers, and supported the recommendations of the American Academy of Pediatrics guidelines.<sup>30</sup> A major question for pediatric nephrologists in developing countries is what strategy should be adopted that can detect silent renal diseases that may manifest later in life. The limitations of our study were that an early morning urine sample was not collected. Repeat evaluation was not done. Further evaluation for the etiology of urinary abnormalities could add significance to the screening of urinary abnormalities in these children.

## CONCLUSION

We concluded that urine screening is the simple and feasible method for diagnosis of urinary abnormalities in asymptomatic children which requires periodic re-evaluation to minimize the progression to chronic renal disease, as treatment of end stage renal disease is a difficult option in our setting due to lack of financial resources and inadequate infrastructure.

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# An Analysis of Colonoscopy Findings in a Tertiary Care Hospital

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## Abstract

**Background:** Around one-fourth of the patients that come to the surgical outpatient department have lower gastrointestinal (GI) symptoms and most of them are not properly evaluated. Colonoscopy is a risk-free simple modality in which the lower GI tract can be visualized until the terminal ileum. It also has the added advantage that certain procedures can be done such as biopsy and polypectomy.

**Methods:** This was a retrospective study. Data on patients who underwent colonoscopy from March 2012 to March 2015 was evaluated; data were collected from the endoscopy register.

**Results:** About 580 patients who underwent colonoscopy during the 3-year period were evaluated. 86% of the patients tolerated the procedure under local anesthesia. Cecum could be reached in the majority (72%) of the patients. The most common indication was found out to be bleeding per rectum (37.9%). Hemorrhoids were the most common lesion found on endoscopy (23%). Most of the pathology was localized to the rectum and anal canal (34.8%). Carcinoma was proven histopathologically in 43 patients out of which 41 had adenocarcinoma, mostly arising from the rectosigmoid area. Polypectomy was successfully done in 20 patients with only one patient having rebleeding after the procedure.

**Conclusion:** Colonoscopy is a safe and effective procedure for diagnosing lower GI symptoms and should be an integral part of management.

**Key words:** Bleeding per rectum, Carcinoma, Chronic diarrhea, Colonoscopy, Polypectomy

## INTRODUCTION

Colonoscopy or coloscopy is the endoscopic examination of the large bowel and the distal part of the small bowel with a fiber optic camera on a flexible tube passed through the anus.<sup>1</sup> It can provide a visual diagnosis (e.g., ulceration, polyps) and grants the opportunity for biopsy or removal of suspected colorectal cancer lesions.

Conditions that warrant colonoscopies include lower gastrointestinal (GI) hemorrhage, unexplained changes in bowel habit and suspicion of malignancy.<sup>2</sup> Colonoscopies are

often used to diagnose colon cancer but are also frequently used to diagnose inflammatory bowel disease. In older patients (sometimes even younger ones) an unexplained drop in hematocrit is an indication for colonoscopy, usually along with an esophagogastroduodenoscopy, even if no obvious blood has been seen in the feces.

Fecal occult blood is a quick test which can be done to test for microscopic traces of blood in the stool. A positive test is almost always an indication to do a colonoscopy.<sup>3</sup> In most cases the positive result is just due to hemorrhoids; however, it can also be due to diverticulosis, inflammatory bowel disease (Crohn's disease, ulcerative colitis), colon cancer, or polyps. Polypectomy has become a routine part of colonoscopy, allowing for quick and simple removal of polyps without invasive surgery.<sup>4</sup>

Hundreds of patients every year undergo colonoscopy in K. R. Hospital for various indications. No data was available correlating the clinical features with the colonoscopic

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findings. Hence, this study was done to analyze the role of colonoscopy in diagnosing lesions in patients who presented with lower GI symptoms.

## MATERIALS AND METHODS

It was a retrospective study carried out from March 2012 to March 2015 in K. R. Hospital, Mysore. K. R. Hospital is a tertiary care hospital located in the heart of Mysore, Karnataka. It serves mostly lower socioeconomic status patients.

### Patients and Exclusion

A total of 620 patients underwent colonoscopy from March 2012 to March 2015. Data on patients who underwent the procedure was collected from the registry. Informed consent was taken from each patient, and ethical clearance was obtained from the ethics committee of Mysore medical college and research institute. All patients in which the colonoscopy was abandoned because of inadequate bowel preparation were excluded from the study. Patients who underwent repeat colonoscopies were excluded. Finally, the patients who could not tolerate the procedure because of the pain were excluded subsequently.

### Data Recording and Statistics

Data were obtained from the colonoscopy register maintained in the endoscopy room. Recorded information included demographic data (age, sex), indication for colonoscopy, preparation used for bowel lavage, type of anesthesia used, endoscopic findings, extent reached, procedure done, and histopathology (if done).

Biopsies were done at the discretion of the endoscopist. The pathological examination was done by an expert pathologist. The data were analyzed and reported in the form of tables and graphs.

## RESULTS

A total of 620 patients underwent colonoscopy over the 3-year period. Data were collected from 580 patients after excluding the rest using the exclusion criteria.

### Patient Characteristics

384 patients (65.51%) were male, 196 (33.79%) female (Graph 1). Age ranged from 16 to 84 years with mean  $43 \pm 15$ . Bleeding per rectum was the most common indication (37.9%). The second most common indication was chronic diarrhea (17%) followed by clinical suspicion of irritable bowel syndrome (13.7%). The various indications for which colonoscopy was done is mentioned in Table 1. 500 patients underwent colonoscopy under local anesthesia with monitoring of pulse and oxygen saturation. Rest 80 patients (age group 16-24) needed sedation with

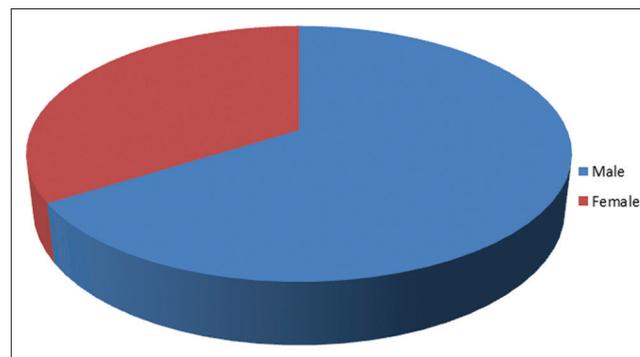
monitoring which was decided beforehand. All patients were prepared with a 1 day prior low roughage diet, laxative at night, and polyethylene glycol bowel purgative.

### Colonoscopy Findings

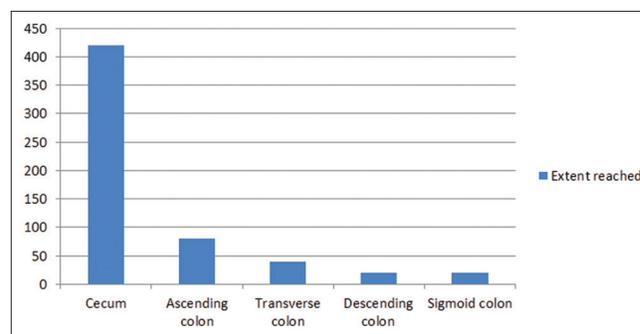
Colonoscopy was done until the cecum in 420 patients (72.4%). In 3.4% of the patients the scopy was done only until the sigmoid colon. The extent reached has been shown in Graph 2. Hemorrhoids was the most common finding in endoscopy (23.1%) followed by polyp (14.4%). 25% of the patients had a normal study. The various lesions found have been tabulated (Table 2). Colonoscopic picture of polyps is shown in Figures 2 and 3. Most of the lesions were found to be in the Rectum and anal canal (34.8%) followed by sigmoid colon (86%). Cecum had 18.75% of lesions. The location of the lesions and the relative frequency has been tabulated (Table 3). 164 lesions were sent for histopathology (excluding polyps),

**Table 1: Indications for colonoscopy**

Indications	n (%)
Per rectal bleeding	144 (24.8)
Irritable bowel syndrome	100 (17.2)
Alteration of bowel habits	87 (15)
Anaemia for evaluation	86 (14.82)
Chronic diarrhoea	79 (13.62)
Pain	44 (7.58)
Constipation	24 (4.13)
Mass lesion	16 (2.75)
Total	580 (100)



**Graph 1: Sex ratio**



**Graph 2: Extend reached**

and 41 lesions turned out to be carcinoma. 39 lesions were adenocarcinoma (95.1%), one melanoma, and

one squamous cell carcinoma. Colonoscopy picture of growth in the sigmoid colon is shown in figure and anal canal melanoma is shown in Figures 4 and 5. Carcinoma was found mostly in the rectum (18 patients), followed by sigmoid colon (Figure 1) (8). The histopathological

**Table 2: Findings in colonoscopy**

Findings	n (%)
Haemorrhoids	134 (23.1)
Polyp	84 (14.4)
Non-specific colitis	74 (12.75)
Ileocecal TB	63 (10.86)
Carcinoma	41 (7.06)
Ulcerative colitis	20 (3.44)
Miscellaneous (diverticulum, stricture, increased hyperemia)	15 (2.58)
Normal	149 (25.68)
Total	580 (100)

TB: Tuberculosis

**Table 3: Pathological site of lesion**

Site of lesion	n (%)
Rectum and anal canal	145 (34.8)
Sigmoid colon	86 (20.67)
Cecum	78 (18.75)
Descending colon	45 (10.8)
Ascending colon	40 (9.61)
Transverse colon	22 (5.28)
Total	416 (100)

164 patients had normal study

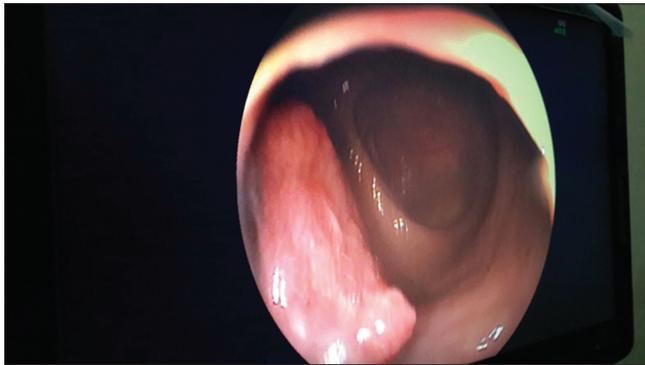


Figure 1: Proliferative growth in sigmoid colon



Figure 4: Anorectal melanoma

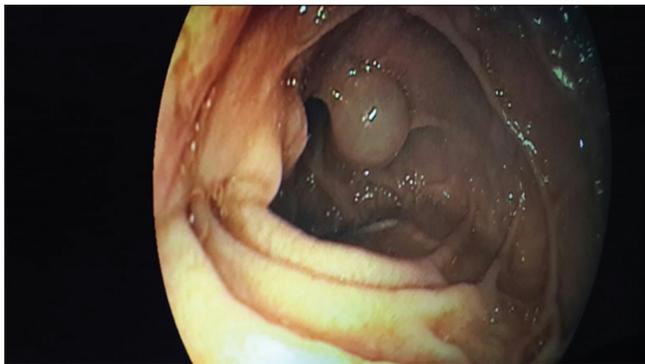


Figure 2: Polyp descending colon

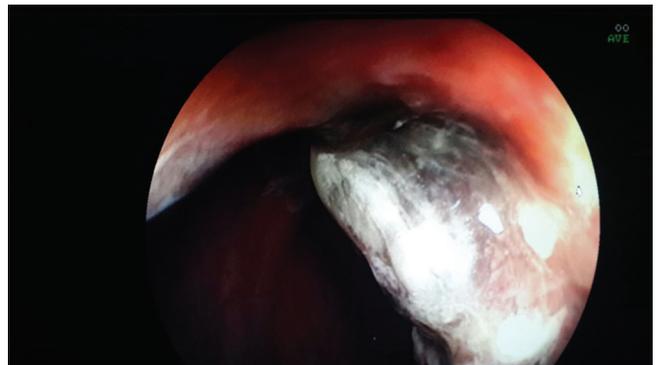
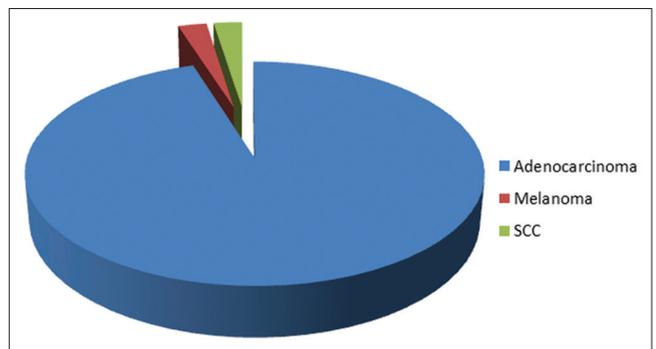


Figure 5: Anorectal melanoma (2<sup>nd</sup> pic)



Figure 3: Polyp transverse colon



Graph 3: Histopathology

picture has been demonstrated in Graph 3. Polypectomy was done in 20 patients and histopathology of polyp showed hyperplastic polyp in 10 patients, villous in five, tubular in 4 and tubulovillous in one patient. One patient had recurrent bleeding after polypectomy which stopped with conservative management. Coming to individual indications, most common cause identified in bleeding per rectum patients was hemorrhoids; 92 patients (63.8%) followed by polyp (27.7%). Carcinoma accounted for 4 cases of bleeding. Patients with irritable bowel syndrome and altered bowel habits had normal study in 64.1% of the cases. Most common lesion identified was non-specific colitis (16%) followed by tuberculosis (TB) (9%). Cause of anemia was found out to be hemorrhoids in 48.8% of the patients. In patients with chronic diarrhea the most common finding was non-specific colitis (40.2%) followed by ulcerative colitis in 4 patients.

## DISCUSSION

Colonoscopy in an established procedure in the work up and screening of patients with lower GI symptoms.<sup>5-7</sup> The demand for colonoscopy has been increasing over the years given the relative safety and the low complication rate associated with the procedure.<sup>8-10</sup>

The American cancer society recommends, starting at the age of 50 years, for both men and women that they undergo a flexible sigmoidoscopy every 5 years or a colonoscopy every 10 years.<sup>11</sup> People with a family history of colon cancer are often first screened during their teenage years. Among people who have had an initial colonoscopy that found no polyps, the risk of developing colorectal cancer within 5 years is extremely low. Therefore, there is no need for those people to have another colonoscopy sooner than 5 years after the first screening.<sup>12,13</sup> Colonoscopy screening prevents approximately two-thirds of the deaths due to colorectal cancers on the left side of the colon, and is not associated with a significant reduction in deaths from right-sided disease.<sup>1</sup>

Colonoscopy is similar to sigmoidoscopy the difference being related to which parts of the colon each can examine. A colonoscopy allows an examination of the entire colon (1200-1500 mm in length). A sigmoidoscopy allows an examination of the distal portion (about 600 mm) of the colon, which may be sufficient because benefits to cancer survival of colonoscopy have been limited to the detection of lesions in the distal portion of the colon.<sup>2,3</sup>

Five in 1000 people who have a colonoscopy have a serious complication.<sup>14</sup> Perforation of the colon occurs at a rate of about 1 in 1000 procedures, and death at a rate of 1 in 3300

to 1 in 333000; therefore, in some low-risk populations, screening in the absence of symptoms would not outweigh the risks of the procedure. In a 2006 study of colonoscopies done from 1994 to 2002, Levin *et al.*, found serious complications occurred in 5.0 of 1000 colonoscopies,<sup>14</sup> comprising 0.8 in 1000 colonoscopies without biopsy or polypectomy, and a rate of 7.0/1000 for colonoscopies with biopsy or polypectomy; although McDonnell and Loura criticize this rate as being unacceptably high.<sup>15</sup> During colonoscopies where a polyp is removed (a polypectomy), the risk of complications has been higher, although still very uncommon, at about 2.3%.<sup>16</sup> One of the most serious complications that may arise after colonoscopy is the postpolypectomy syndrome. This syndrome occurs due to potential burns to the bowel wall when the polyp is removed. It is, however, a very rare complication and as a result patients may experience fever and abdominal pain. The condition is treated with intravenous fluids and antibiotics while the patient is recommended to rest.

This study highlights several features observed on colonoscopy. The male:female ratio is inconsistency with other studies.<sup>17</sup> It has been observed that there are more indications in men than women for undergoing colonoscopy. Age wise it has been seen that colonoscopy has been done more for adult patients (mean age 45) which is not consistent with other studies where the younger population was involved.<sup>17</sup>

The indications that were evaluated were similar to what other studies revealed with the most common indication in our study being bleeding per rectum with a yield of 72%.<sup>18</sup> Hemorrhoids were the most common cause found for such bleeding and is consistent with the review of the literature.<sup>19</sup>

Cecum was the extent reached in 72% which is similar to other studies.<sup>20</sup> Most of the lesions were limited to the rectum and anal canal, the reason being that hemorrhoids was the most common lesion found in the study.

Colorectal cancer was identified in 41 patients after histopathological examination. That is a significant percentage as compared to other studies.<sup>21</sup> The increased incidence of carcinoma in our study could be attributed to the increased mean age of patients and also considering the fact that K. R. hospital mainly tenders to the lower socioeconomic population. Most patients come at a late stage where carcinoma is advanced. One single case of anal canal melanoma was also identified but most other carcinomas where adenocarcinoma, mostly arising from the rectum or the sigmoid colon. In patients who came with evaluation of chronic anemia right-sided colonic cancer was found out to be more, as anemia is usually the presentation of right-sided colonic tumors.

Patients who came with mass per abdomen had a more of TB picture, which was confirmed by histopathology. Carcinoma was identified only in a few patients. This highlights the need for early colonoscopy in patients especially in the elderly where early carcinoma can be diagnosed.

The limitations of the study included lack of facility to do colonoscopy under sedation in all the cases, hence many patients were excluded because they couldn't tolerate the pain and the study were hence abandoned and was referred elsewhere. Furthermore, around two surgeons did the colonoscopy; hence there could have been observer bias and bias in taking decision for biopsy.

## CONCLUSION

Colonoscopy forms an important modality in the workup for a patient presenting with lower GI symptoms. As seen in our study the yield is significant with only a few cases having a normal study. Case selection and stratification of patients based on the need can further increase the yield. It is a simple procedure, can be done under local anesthesia or under mild sedation. Records can be kept to see how the lesions react to further therapy. Added advantage of colonoscopy is that therapeutic procedures like polypectomy, removal of foreign body can be done with minimal risk. It was also a safe study as proven in our study with minimal complications and post study pain.

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# Nutritional Status of Anganwadi Children under the Integrated Child Development Services Scheme in a Rural Area in Goa

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## Abstract

**Background:** Childhood malnutrition is a leading cause of child morbidity and mortality.

**Objective:** Of the study was to estimate the prevalence of malnutrition in terms of underweight, stunting, and wasting in children aged 6 months-6 years (72 months) registered in Anganwadi Centers (AWCs) in a rural area of Goa.

**Methods:** A cross-sectional study was conducted from January 2015 to June 2015 in rural area in Goa. A total of 782 registered beneficiary children aged 6 months-6 years (72 months) from AWCs were selected by simple random sampling.

**Results:** The overall prevalence of underweight, wasting, and stunting in the study population was found to be 33.4%, 24%, and 31.5%, respectively. Severe malnutrition (below -3 standard deviation cut-off) was found in the study population, with 9.2% of children severely underweight, 10.4% severely wasted, and 8.7% severely stunted. It was observed that the proportion of underweight children in the age group of 6-36 months was higher (38.1%) than the proportion of underweight children (24.9%) in the age group of 37-72 months, and this difference was found to be statistically significant ( $\chi^2 = 14.13$ ,  $P = 0.0001$ ). The proportion of underweight children was found to be the highest (51.3%) in lower class, and lowest (17.1%) in upper class and a statistically significant association between socio-economic class and nutritional status ( $\chi^2 = 37.02$ ,  $P = 0.000$ ) was found.

**Conclusion:** Malnutrition continues to be a major problem in children below 6 years of age. Though the Integrated Child Development Services Scheme is taking measures to combat this problem, India's progress in reducing child malnutrition has been slow. However, continuous monitoring and surveillance of AWCs could help in the planning of preventive strategies.

**Key words:** Anthropometry, Child, Nutritional status, Preschool, Protein - energy malnutrition

## INTRODUCTION

Malnutrition in children is a silent emergency leading to almost seven million child deaths (approximately 55% of all child deaths) annually.<sup>1</sup> Globally, 26% of children are moderately to severely underweight, 10% are moderately to severely wasted, and 31% are moderately to severely stunted.<sup>1</sup>

In India, 48% of children under 5 years are stunted and 43% are underweight and 20% of children under 5 years in the country are wasted.<sup>2</sup> Failing to deal effectively with the malnutrition problem in India has dire consequences for children's development. Through precipitating disease and speeding its progression, malnutrition is a leading contributor of infant and child mortality and morbidity. More than half (54%) of all deaths before the age of 5 years in India are related to malnutrition. Due to the extensive prevalence in India, mild to moderate malnutrition contributes to more deaths (43%) than severe malnutrition (11%).<sup>2</sup>

Recognizing the extensive prevalence of malnutrition and the consequent drain on the country's human resource, the Government of India started the Integrated Child

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Development Services (ICDS) Scheme; to respond to the child's needs in a comprehensive and holistic perspective. The ICDS Scheme adopts integrated approaches that incorporate nutrition and health together with early opportunities for cognitive and social stimulation. Food supplements are given to beneficiary children to meet their part calorie requirements and to supplement their dietary intake.

The nutritional status of children can be evaluated by their growth. Children with undernutrition as one form of malnutrition, are being recognized as a vulnerable category for focused action. Undernutrition has been measured by anthropometric indicators in terms of stunting, wasting, and underweight. Stunting (low height for age) and wasting (low weight for height) are respectively associated with chronic malnutrition and current nutritional status. Underweight (low weight for age) represents both chronic and acute malnutrition.

### Program Description

The Government of India started ICDS Scheme, a centrally sponsored scheme to enhance the health, nutrition, and learning opportunities of children <6 years of age especially targeted for the poor and the deprived. Under the ICDS Scheme, Anganwadi Centers (AWCs) are the focal point for the delivery of services and are run by the local community woman, the Anganwadi Worker (AWW) and a helper. Freshly, cooked food supplements are provided at all AWCs to children aged 3-6 years while take-home-rations of food grains are provided every month to children aged 6 months until 3 years (36 months). All children in the eligible age groups can avail of supplementary nutrition provided at the AWCs.

Weighing of each child is carried out by the AWW every month and plotted on the growth chart which is a graphical presentation of weight-for-age. Through the strategy of Nutrition and Health Education, ICDS Scheme aims at bringing about an attitudinal change in health and nutrition habits of the mothers and children and improve their nutritional status. Despite the expansion of the ICDS Scheme to cover to cover most of the children in the country, progress in reducing child malnutrition has been slow.<sup>3</sup>

### Objective of the Study

To assess the prevalence of malnutrition in terms of underweight, wasting, and stunting in children aged 6 months-6 years (72 months) of age registered in AWCs in rural area in Goa.

## METHODS

### Study Design

A cross-sectional study was conducted from January 2015 to June 2015.

### Study Setting and Period

The study was conducted from January 2015 to June 2015, in rural areas of Rural Health and Training Centre, Mandur, which is the rural field practice area of Goa Medical College, a tertiary care hospital in Goa.

### Study Participants

The study participants consisted of registered beneficiary children aged 6 months-6 years (72 months) of age from AWCs, which were selected by simple random sampling.

### Sample Size and Sampling Technique

Sample size<sup>3</sup> was calculated as follows

$$\begin{aligned} \text{Sample size} = n &= \frac{1.96^2 p(1-p)(DEFF)}{d^2} \\ &= \frac{1.96^2 \times .5 \times .5(2)}{.05^2} = 768.32 \end{aligned}$$

Wherein assuming estimate of the expected proportion ( $p$ ) = 0.5, desired level of absolute precision ( $d$ ) = 0.05, and estimated design effect ( $DEFF$ ) = 2: Hence, minimum sample required for the study was calculated.

A list of AWCs and the number of registered beneficiary children aged 6 months-6 years (72 months) attending them was obtained from the Department of Women and Child Development, Goa. From this list, 16 AWCs were selected by simple random sampling, based on calculated sample size; and all registered beneficiary children aged 6 months-6 years (72 months) of age from these selected AWCs were recruited in the study giving a sample size of 782.

### Inclusion Criteria

Registered beneficiary children aged 6 months-6 years (72 months) of age from selected AWCs.

### Exclusion Criteria

Registered beneficiary children aged 6 months-6 years (72 months) of age whose parents did not consent to being part of the study, and/or who were very sick or those who were unavailable at 2 consecutive visits were excluded from the study.

### Data Collection

Data regarding selected variables and anthropometric measurements were collected using a predesigned structured questionnaire, Mother of the child was chosen as the preferred responder, if the mother was not available then the father or grandparent was chosen as a responder. The exact age in months was computed from the child's date of birth as per birth certificate, or as told by the respondent. The respondents were asked for information regarding family income. The Socioeconomic status was determined by using modified Prasad's scale.<sup>4</sup>

### Anthropometry

Anthropometric measurements were carried out following standard methods.<sup>5</sup> The data included weight, recumbent length (for children <24 months of age), and height (for children more than 24 months of age). Weight was measured to the nearest 0.1 kg and Salter weighing machine was used for weight measurement. Height was measured against a nonstretchable tape fixed to a vertical wall, with the participant standing on a firm/level surface and it was measured to the nearest 0.5 cm. Recumbent length (for children <24 months of age) was measured with a wooden length board.

### Assessment of Nutritional Status

The nutritional status of children was assessed by plotting weight and height of the children on WHO 2006 Growth Standards growth charts using z-scores.<sup>6,7</sup> Undernutrition, as one form of malnutrition, has been measured by anthropometric indicators - Underweight (low weight for age, W/A), Stunting (low height for age, H/A), and Wasting (low weight for height, W/H).<sup>3,4</sup> Children falling below -2 standard deviation (SD) cutoff were considered as follows; underweight - weight for age, W/A < -2 SD; stunting - height for age, H/A < -2 SD; wasting - weight for height, W/H < -2 SD. Severe underweight, W/A < -3 (SD); severe stunting, H/A < -3 SD; severe wasting, W/H < -3 SD.

### Statistical Analysis

Data were analyzed using Epi-Info 7 software, and appropriate statistical tests were applied.

### Ethical Consideration

Informed verbal consent was taken from the parents of the study subjects.

## RESULTS

A total of 782 children aged 6 months-72 months registered in 16 AWCs were recruited in the study. It can be seen in Table 1, that 64% of the study population comprised of children aged 6-36 months, and 36% were between the ages of 37 and 72 months. The study population comprised of 50.4% boys and 49.6% girls.

**Table 1: Age and gender distribution of the study population**

Age group (months)	n (%)		Total
	Male	Female	
6-36	252 (50.3)	249 (49.7)	501 (64)
37-72	142 (50.5)	139 (49.5)	281 (36)
Total	394 (50.4)	388 (49.6)	782 (100)

In Table 2, it is observed that the overall prevalence of underweight, wasting, and stunting in the study population was found to be 33.4%, 24%, and 31.5% respectively. The prevalence of mild to moderate underweight, mild to moderate wasting, and mild to moderate stunting in the study population was found to be 24.2%, 13.6%, and 22.8%, respectively. Severe malnutrition (below -3SD cut off) was found in the study population, with 9.2% of children found to be severely underweight, 10.4% were found to have severe wasting, and 8.7% of children were found to be severely stunted.

In Table 3, it was observed that the proportion of underweight children in the age group of 6 months to 36 months was higher (38.1%) than the proportion of underweight children (24.9%) in the age group of 37-72 months, and this difference was found to be statistically significant ( $\chi^2 = 14.1373$ ,  $P = 0.0001$ ). It was observed that 35.1% of girls were underweight, and 31.7% of boys were underweight, but this difference was not found to be statistically significant. It was observed that the proportion of underweight children was found to be the highest (51.3%) in lower class; followed by 30.6% in upper lower; 28% and 32.8% in lower middle and upper middle class, respectively; and lowest (17.1%) in upper class, and this difference was found to be statistically significant ( $\chi^2 = 37.02$ ,  $P = 0.000$ ).

## DISCUSSION

In the present study, it was observed that the overall prevalence of underweight, wasting, and stunting in the study population was found to be 33.4%, 24%, and 31.5%, respectively. Severe malnutrition (below -3 SD cutoff) was found in the study population, with 9.2% of children were found to be severely underweight, 10.4% were found to have severe wasting and 8.7% of children were found to be severely stunted. Several studies in various states of India have reported different rates of malnutrition which depends on various developmental conditions of that region. A study conducted in Assam<sup>8</sup> found that the overall prevalence of underweight, stunting, and wasting was found to be 29%, 30.4%, and 21.6%, respectively. Severe underweight, stunting, and wasting (<-3 SD) was found in 10.6%, 7.0%, and 8.6%, respectively. A study conducted in Bareilly, Uttar Pradesh; reported that 53.86% children were underweight, 43.22% children were stunted, and 60.67% were wasted.<sup>9</sup> As per a survey of the nutritional status of preschool children, in a rural population of Lucknow,<sup>10</sup> 53.86% children were underweight, 43.22% children were stunted, and 60.67% were wasted. Some of the studies cited above<sup>9,10</sup> have higher rates of malnutrition as compared to the present study. Lower rates of malnutrition in the present

**Table 2: Prevalence of underweight, stunting and wasting in study population based on the WHO child growth standards**

WHO 2006 growth standards	Indicators of nutritional status								
	Underweight			Wasting			Stunting		
	Male	Female	Total	Male	Female	Total	Male	Female	Total
Severe (below - 3 SD)	34 (8.6)	38 (9.8)	72 (9.2)	38 (9.7)	43 (11)	81 (10.4)	32 (8.2)	36 (9.3)	68 (8.7)
Mild to moderate (below - 2 SD)	91 (23.1)	98 (25.3)	189 (24.2)	52 (13.1)	55 (14.2)	107 (13.6)	88 (22.3)	90 (23.2)	178 (22.8)
Normal (>median to -2SD)	269 (68.3)	252 (64.9)	521 (66.6)	304 (77.2)	290 (74.8)	594 (76)	274 (69.5)	262 (67.5)	536 (68.5)
Total	394 (100)	388 (100)	782 (100)	394 (100)	388 (100)	782 (100)	394 (100)	388 (100)	782 (100)

(Numbers in parenthesis indicate percentages), SD: Standard deviation

**Table 3: Association of socio-demographic variables with nutritional status**

Socio demographic variables	Nutritional status		OR (95%CI)	P value
	Number	Underweight		
Age group (months)				
6-36	501	191 (38.1)	310 (61.9)	1.85 (1.34-2.57)
37-72	281	70 (24.9)	211 (75.1)	1 (ref)
Gender				
Male	394	125 (31.7)	269 (68.3)	0.86 (0.63-1.16)
Female	388	136 (35.1)	252 (64.9)	1 (ref)
Socioeconomic class				
Class I (upper)	82	14 (17.1)	68 (82.9)	1 (ref)
Class II (upper middle)	204	67 (32.8)	137 (67.2)	2.37 (1.24-4.52)
Class III (middle)	189	53 (28)	136 (72)	1.89 (0.98-3.65)
Class IV (lower middle)	147	45 (30.6)	102 (69.4)	2.14 (1.09-4.20)
Class V (lower)	160	82 (51.3)	78 (48.7)	5.10 (2.65-9.81)

SD: Standard deviation, OR: Odd ratio, CI: Confidence interval

study could probably be due to high female literacy rate and higher per capita expenditure on health in the State of Goa.<sup>11</sup>

The present study reports that there was no statistically significant difference in proportions of underweight boys and girls. Similar findings were reported in a study conducted by Banerjee *et al.*<sup>12</sup> wherein malnutrition was more common in females than males, but this was not significant ( $P > 0.05$ ). Contrary to this, other studies have found higher proportion of malnutrition in boys; wherein 67.4% boys and 61.58% girls were found to be malnourished in a study conducted by Ray *et al.*<sup>13</sup> as also, in a study conducted in Andhra Pradesh,<sup>14</sup> where 80% boys were poorly nourished as compared to 75% of girls.

In the present study, the proportion of underweight children in the age group of 6-36 months was higher (38.1%) than the proportion of underweight children (24.9%) in the age group of 37-72 months, and this difference was found to be statistically significant. Similarly, Ray *et al.*<sup>13</sup> reported that the prevalence of malnutrition was highest (74.19%) in the age group 12-23 months followed by 66.18% in the age group 24-35 months and 60.47% in the age group 36-59 months.

In the present study, it was observed that the proportion of underweight children was found to be highest (51.3%) in lower class, and lowest (17.1%) in upper class. It was found that prevalence of underweight children was higher among children in lower socioeconomic class as compared to those from higher socioeconomic class and this association was found to be statistically significant. Similar findings were observed in a study conducted in Uttar Pradesh, India, where it was observed that prevalence of under-nutrition was higher among children from low-income group as compared to higher income group, however, the association was not found significant ( $\chi^2 = 2.48$ ,  $df = 4$ ,  $P > 0.1$ ),<sup>9</sup> as also reported by Dhakal *et al.*,<sup>15</sup> wherein the 82.75% children with malnutrition were from the low-income group, i.e., IV and V by Prasad Scale.

## CONCLUSION

The overall prevalence of under-nutrition in the study population was assessed and severe undernutrition was found to be present. Malnutrition continues to be a major problem in children below 6 years of age. Though the ICDS Scheme is taking measures to combat this problem, India's progress in reducing child malnutrition has been

slow. However, continuous monitoring and surveillance of AWCs could identify underlying factors of malnutrition, thus help in the planning of preventive strategies.

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# Comparative Study of Lipid Profile in Normotensive and Hypertensive Pregnant Women

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## Abstract

**Introduction:** Hypertension (HTN) during pregnancy is one of the leading causes of maternal and perinatal morbidity and mortality. Dyslipidemia is critical in the pathogenesis of endothelial dysfunction. There are a very few studies in this regard from South India. This study compared lipid levels in the hypertensive and normotensive pregnant women and correlated them with the maternal outcome.

**Methods:** This was a prospective, comparative study done at JSS hospital, a tertiary care teaching hospital in Mysore city between December 2012 and April 2014. About 70 patients with HTN in pregnancy, and 70 age-matched normotensive pregnant controls were taken up and lipid levels were analyzed statistically.

**Results:** The majority of the pregnant patients were in the age group of 21-25 years (47.1%) with a mean age of 22 years. The primigravida were 76 (54.3%), the second and third gravida 49 (35%) and 14 (10%), respectively. The mean values of total cholesterol in normotensives was 172 (Standard deviation [SD]  $\pm$  40.8) mg/dl and in hypertensive 279.5 (SD  $\pm$  73.2)  $P$  < 0.0001. Mean high density lipoprotein-cholesterol in the hypertensives was 43.3 mg/dl (SD  $\pm$  15.4) and in normotensives 53 mg/dl (SD  $\pm$  11.3)  $P$  < 0.0001. Low-density lipoprotein-cholesterol (LDL-C) was significantly increased in hypertensives - mean 162.4 mg/dl (42.8) and 88.4 (SD  $\pm$  30.3) mg/dl in normotensives  $P$  < 0.0001. Very LDL-C was significantly increased in hypertensives with mean 68.3 mg/dl (SD  $\pm$  27.9) mg/dl while in normotensives it was 28.7 mg/dl (SD  $\pm$  11.3). Hypertensive patients had a mean triglycerides (TG) of 290.7 mg/dl (SD  $\pm$  126.5) while in normotensive mean TGs was 152.8 mg/dl (SD  $\pm$  48.4)  $P$  > 0.0001. 25 (35.7%) in the hypertensive group had full term normal delivery compared to 46(65.7%) normotensive patients  $P$  = 0.001. 45 (64.3%) in the hypertensive group had caesarean section compared to 24 (34.3%) in the normotensive group  $P$  = 0.001.

**Conclusions:** The lipid profile parameters were significantly abnormal in hypertensive pregnant patients. Significantly, the more hypertensive pregnancies with dyslipidemia underwent caesarean section Serum lipid levels should be monitored in pregnancy to prevent obstetric complications.

**Key words:** Cesarean, Endothelial dysfunction, Hypertension, Lipid profile, Preeclampsia

## INTRODUCTION

Hypertension (HTN) during pregnancy is a major health problem. It is the one of the leading causes of maternal and perinatal morbidity and mortality.<sup>1</sup> Lipid values in normal pregnancies change with gestational age. HTN and dyslipidemia are major risk factors for cardiovascular

disease (CVD) and account for more than 80% of deaths and disability in low- and middle- income countries. It is widely accepted that CVD is associated with HTN and increased blood levels of low-density lipoprotein (LDL), total cholesterol (TC), and triglycerides (TGs).<sup>2,3</sup> In contrast, a low level of high-density lipoprotein (HDL) is a risk factor for mortality from CVD.<sup>4</sup> In a normotensive pregnancy serum TGs, TC and HDL increase during pregnancy but lipoprotein A level decreases. These changes are reported to be secondary to hormonal changes during pregnancy.

Preeclampsia (PE) is a leading cause of morbidity and mortality in pregnant women. It is characterized by HTN and an increased systemic inflammatory response

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potentially initiated by widespread endothelial damage dysfunction. Women with PE demonstrate marked dyslipidemia. It has been observed that the concentration of serum TC, serum TGs, HDL-cholesterol (HDL-C), and LDL-cholesterol (LDL-C) in normal pregnant women increased with increasing age.<sup>5</sup> Most of the available literature is from Western sources carried out on Caucasian populations. Ethnic variations in lipid parameters are well recognized. There are very few studies in this regard from India more so the Southern region of India. Hence, there was a need to study the lipid profile changes in hypertensive pregnant women in comparison with normotensive pregnant women.

### Objective of the Study

The primary objective was to compare the lipid profile in hypertensive and normotensive pregnant women, and the secondary objective was to note the maternal outcome with lipid profile changes.

## MATERIALS AND METHODS

This was a prospective hospital-based comparative study of antenatal cases admitted in Obstetrics Department, JSS hospital, a tertiary care teaching hospital attached to JSS University carried out between December 2012 and April 2014. HTN in pregnancy was defined as blood pressure (BP) 140/90 mm of Hg. 70 Ante-natal hypertensive cases were and 70 normotensive pregnant were enrolled. The hypertensive pregnant group included gestational HTN, chronic HTN, PE, superimposed PE and eclampsia. Pregnant patients with gestational diabetes mellitus, obesity and those with family history of hyperlipidemia were excluded from the study.

A blood sample of 3 ml was collected from the subjects after 8-10 h of fasting in a vacutainer not coated with any anticoagulant. The blood was processed in biochemistry lab of JSS hospital to obtain the values of TC, HDL-C, TGs, LDL-C the test method used for TC, HDL-C, LDL-C was enzymatic method and that for TGs is glycerol-3-phosphate oxidase-PAP method. The samples were processed in "Automated Chemistry Analyzer" (Toshiba).

The normal values of lipid profile according to recent National Cholesterol Education Programme Guidelines were taken as follows:

TC: <200 mg/dl, LDL-C: <100 mg/dl, HDL-C: > 40 mg/dl

TGs: 35-<150 mg/dl, very LDL-C (VLDL-C): <30 mg/dl

The study was presented before and cleared by the Institutional Ethical Committee of JSS Medical College.

### Statistical Analysis

The values obtained were compared between the hypertensive and normotensive groups. The Descriptives procedure was used to display univariate summary statistics for several variables in a single table. The Frequencies procedure was used for describing many types of variables. The Crosstabs procedure was used to measure of association for two-way tables. The Chi-square test procedure was used to tabulate variables into categories.  $P < 0.005$  was assessed for statistical significance. All the statistical methods were carried out through the SPSS for Windows (version 16.0).

## RESULTS

The majority of the pregnant patients were in the age group of 21-25 years (47.1%) with a mean age of 22 years. 45 (32.1%) were in 39 weeks of gestation. The primigravida were 76 (54.3%), second and third gravida 49 (35%) and 14 (10%), respectively, (Table 1). Mean values of TC in normotensives was 172. (Standard deviation [SD]  $\pm$  40.8) mg/dl and in the hypertensive group it was 279.5 (SD  $\pm$  73.2)  $P < 0.0001$ . Mean HDLC in hypertensives was 43.3 mg/dl (SD  $\pm$  15.4) and in normotensives was 53 mg/dl (SD  $\pm$  11.3)  $P < 0.0001$ . LDL-C was significantly increased in hypertensives with a mean of 162.4 mg/dl (42.8) while it was 88.4 (SD  $\pm$  30.3) mg/dl in normotensives  $P < 0.0001$ . VLDLC showed a significant increase in hypertensive patients with mean of 68.3 mg/dl (SD  $\pm$  27.9) mg/dl. In normotensives it was 28.7 mg/dl (SD  $\pm$  11.3). Hypertensive patients had a mean TGs of 290.7 mg/dl (SD  $\pm$  126.5) while in normotensive mean TGs was 152.8 mg/dl (SD  $\pm$  48.4)  $P < 0001$  (Tables 2 and 3). 25 (35.7%) in the hypertensive group had full term normal delivery compared to 46 (65.7%) normotensive patients  $P = 0.001$ . 45 (64.3%) in the hypertensive group had lower segment caesarian section compared to 24 (34.3%) in the normotensive group  $P = 0.001$  (Table 4).

**Table 1: Distribution of patients according to their age, BMI, POG in both hypertensive and normotensive state**

Patient parameter	n	Mean $\pm$ SD	P value
Age (years)			
Normotensive	70	24.5942 $\pm$ 3.46121	0.2
Hypertensive	70	25.4429 $\pm$ 3.54939	
BMI (kg/m <sup>2</sup> )			
Normotensive	70	21.6377 $\pm$ 2.19606	0.7
Hypertensive	70	21.5286 $\pm$ 1.51056	
POG_weeks			
Normotensive	70	39.17 $\pm$ 1.014	0.09
Hypertensive	70	38.19 $\pm$ 4.750	

BMI: Body mass index, POG: Periods of gestation, SD: Standard deviation

## DISCUSSION

CVD in non-pregnant is directly associated with increased levels of TC, TGs, LDL and VLDL whereas, at the same time, the levels of HDL are decreased. TC, TGs, LDL, and VLDL are known as bad cholesterol as they play their destructive role in several diseases.

In early pregnancy, it has been shown that altered levels of serum lipids increase the risk of pregnancy-induced HTN (PIH).<sup>6,7</sup> Pregnant women are having HTN usually have higher levels of TC, TGs, LDL, and VLDL whereas, the levels of HDL are decreased as compared to that in normal pregnant women.<sup>8</sup> In the present study, we investigated the correlation of lipid levels with the systemic BP throughout the pregnancy period. Normotensive pregnant women were taken as a control group and hypertensive pregnant women as a study group. The mean age was 22 years in both the study group and control group.

In the hypertensive group, it was noted that TC, LDL, VLDL and TGs were statistically significantly higher in the hypertensive group whereas there was no significant statistical difference in the levels of HDLC between the two groups. The results of our study are consistent with that of Wald *et al.*<sup>9</sup>

**Table 2: Lipid profile values in hypertensive and normotensive state**

Lipid parameter	n	Mean±SD	P
TC (mg/dl)			
Normotensive	70	172.9565±40.74398	<0.0001
Hypertensive	70	259.9143±76.61852	
HDL (mg/dl)			
Normotensive	70	53.0290±11.35130	<0.0001
Hypertensive	70	43.3286±14.72917	
LDL (mg/dl)			
Normotensive	70	88.4493±30.47107	<0.0001
Hypertensive	70	154.6857±47.98688	
VLDL (mg/dl)			
Normotensive	70	28.7681±11.38904	<0.0001
Hypertensive	70	65.0000±26.73488	
TGs (mg/dl)			
Normotensive	70	152.8406±48.63115	<0.0001
Hypertensive	70	275.3857±123.24858	

TC: Total cholesterol, HDL: High-density lipoprotein, LDL: Density lipoprotein-cholesterol, VLDL: Very density lipoprotein-cholesterol, TGs: Triglycerides, SD: Standard deviation

The results of our study are similar to the results of study done by Anjum *et al.*<sup>10</sup> in Pakistan. This can be because of the similar ethnicity of the population studied. TC and LDL-C. VLDL TGs components of lipid profile were increased in the hypertensive group when compared with normotensive group, and HDL was significantly lower and their results were comparable to various other studies.<sup>11-15</sup>

Normally, in early, pregnancy altered levels of serum lipid profile increase the risk of PIH. Pregnant women with HTN usually have high levels of TC, TGs, LDL, VLDL, whereas levels of HDL are decreased as compared to that in normotensive pregnant women. PIH may cause several critical problems in pregnancy such as preterm deliveries, intrauterine growth restriction, fetal death, maternal mortality, and morbidity. Several factors responsible for PIH have been identified but among them the most important are lipid components. It has been reported that metabolism of lipoprotein is directly associated with PIH. The association of abnormal lipid values in the promotion of HTN in pregnant women helps to investigate the underlying pathological process of HTN in pregnancy. PIH is characteristically associated hypertriglyceridemia.<sup>16</sup> The principle modulator of hypertriglyceridemia is estrogen which is also associated with hyperestrogenemia during pregnancy. Estrogen induces hepatic production of TGs that causes PIH and endothelial dysfunction through the generation of LDL and VLDL. Endothelial dysfunction is the most important event in the pathogenesis of HTN during pregnancy, and abnormal levels of lipid profile play their critical role in the induction of endothelial dysfunction. The limitation of this study could be the small sample size which might need to be increased in future large-scale similar studies for better results.

## CONCLUSION

Dyslipidemia is more profound in hypertensive pregnant women than in those with normal BP. Lipids may have an important role in the etiopathogenesis of PE. Serum lipid profiles should be monitored during pregnancy.

**Table 3: Mean lipid values in normotensive and various hypertensive state**

Lipid parameter	Normotensives	PE	Gestational HTN	Eclampsia	Chronic HTN	Superimposed PE
TC (mg/dl)	172.3	279.5	228.4	237.0	178	180.5
HDL (mg/dl)	53.1	43.2	44.4	40.3	60	39
LDL (mg/dl)	88.4	162.4	145.8	147.3	100	103
VLDL (mg/dl)	28.7	68.3	57.1	74.3	48	34.5
TGs (mg/dl)	152.4	290.7	251.8	269.8	247	149.5

P<0.0001, HTN: Hypertension, TC: Total cholesterol, HDL: High-density lipoprotein, LDL: Density lipoprotein-cholesterol, VLDL: Very density lipoprotein-cholesterol, TGs: Triglycerides, PE: Preeclampsia

**Table 4: Distribution according to mode-of-delivery in hypertensive state**

Hypertension status	Mode-of-delivery (n (%))		Total
	FTND	LSCS	
Normotensive	46 (65.7)	24 (34.3)	70
PE	13 (28.9)	32 (71.1)	45
Gestational HTN	9 (56.3)	7 (43.8)	16
Eclampsia	1 (16.7)	5 (83.3)	6
Chronic HTN	0 (0.0)	1 (100.0)	1
Superimposed PE	2 (100.0)	0 (0.0)	2
Total	71 (50.7)	69 (49.3)	140

HTN: Hypertension, LSCS: Lower segment caesarian section, FTND: Full term normal delivery, PE: Preeclampsia

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# Diastolic Dysfunction in Young Asymptomatic Diabetic Patients

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## Abstract

**Background:** Heart failure is 2-5 times more common in diabetic subjects than in non-diabetic population and can occur even in the absence of coronary artery disease. The relationship between diastolic function and glycemic control has been a matter of debate and studies have shown that they have no definite relationship. The prognostic importance of subclinical diastolic dysfunction creates the need for early intervention.

**Aim and Objectives:** To study the prevalence of diastolic dysfunction in young asymptomatic diabetic patients and to analyze whether its prevalence varies with glycemic control and duration of diabetes.

**Materials and Methods:** The study included 100 young (<40 years with 50 males and 50 females) diabetic patients in Sri Ramachandra Medical College and Hospital from the year 2011 to 2013. 50 healthy controls under 40 years (25 males and 25 females) were taken. All routine lab parameters, fasting and post-prandial sugars, hemoglobin A1c (HbA1c), chest X-ray, electrocardiogram, and two-dimensional echocardiogram were done for all patients.

**Results:** The overall prevalence of diastolic dysfunction was 30%. Of the 50 females 20 patients (40%) had left ventricular diastolic dysfunction (LVDD), while 10 out of 56 males had LVDD (20%). Among 70 Type II diabetes mellitus (DM) patients, 21 had LVDD (30%) while among 30 Type I DM patients 9 had LVDD (30%). Among 60 patients of <6 months duration of diabetes LVDD was found in 18 patients (30%), of patients who had DM of 6 months-3 years duration, LVDD was found in 9 (30%). Of 10 patients who had DM more than 3 years duration, LVDD was found in 3 patients (30%). 60 patients had good glycemic control and 18 had LVDD. 9 patients with HbA1c between 7 and 8 had LVDD (30%) and 3 with HbA1c >8 had LVDD.

**Conclusion:** Diastolic dysfunction could have no definite relation to duration of diabetes.

**Key words:** Cardiomyopathy, Diastolic dysfunction, Diabetes mellitus, Echocardiography, Glycemic control

## INTRODUCTION

Diastolic left ventricular dysfunction is now increasingly recognized as a condition leading to morbidity, hospitalizations and death. The term “diastolic dysfunction” refers to changes in ventricular diastolic properties that have an adverse effect on stroke volume. Recent studies suggest that isolated diastolic heart failure occurs in 30-60% of all patients presenting to hospitals with evidence of

congestive heart failure (CHF). Diastolic heart failure in diabetes is a unique clinical entity. Several factors have been shown to be predisposing conditions associated with the development of diastolic CHF. The most common of these conditions is hypertension. Studies show that 60% of patients with diastolic CHF are hypertensive. Elevations of blood pressure alter left ventricular diastolic function via several mechanisms, some of which are not well-understood. One of these mechanisms is the development of left ventricular hypertrophy. Coronary artery disease (CAD), even in the absence of infarction, is also associated with the development of the left ventricular diastolic dysfunction (LVDD). Less common conditions associated with diastolic CHF are hypertrophic cardiomyopathy, infiltrative cardiomyopathy such as amyloidosis, and rarely restrictive cardiomyopathies. Ventricular function

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is highly dependent on pre-load as demonstrated by the Frank-Starling relationship. Therefore, if ventricular filling (pre-load) is impaired, this will lead to a decrease in stroke volume. The diagnosis of diastolic heart failure is currently based on the presence of signs or symptoms of the CHF such as dyspnea or orthopnea, documentation of normal or only minimally reduced left ventricular systolic function by cardiac imaging technique, and evidence of abnormalities of left ventricular relaxation. This last criterion is the most difficult to document. The analysis of diastolic function can be complex. Unlike systolic dysfunction, there is no single physiological parameter such as ejection fraction that reliably describes the presence and severity of diastolic problems.

Clinical, epidemiological and pathologic data support the presence of a specific cardiomyopathy related to diabetes mellitus (DM). DM is commonly associated with conditions, such as coronary atherosclerosis and hypertension, which may impair myocardial performance. The existence of a diabetic cardiomyopathy was first suggested by Rubler *et al.*<sup>1</sup> in 1972 on the basis of post-mortem findings in four diabetic adults who had CHF in the absence of atherosclerotic, valvular, congenital, hypertensive, or alcoholic heart disease. Diabetic women were especially vulnerable, having congestive, heart failure at twice the frequency experienced by men irrespective of CAD status. The role of severity or duration of diabetes in the development of CHF was not addressed in this study. Further support for the existence of a diabetic cardiomyopathy was provided by Hamby *et al.*, who noted an increased incidence of diabetes in patients with idiopathic cardiomyopathy. Regan<sup>2</sup> described the angiographic and hemodynamic findings in patients with adult-onset diabetes without hypertension or valvular disease.

Since no myocardial ischemia could be demonstrated, abnormalities of the small arteries or capillaries were thought to be responsible for a restriction in myocardial perfusion. Hemodynamic findings included a modest elevation of left ventricular end diastolic pressure and a reduction in both stroke volume and ejection fraction. Ventricular compliance was found to be significantly diminished. A similar impairment of left ventricular compliance was discovered in eight diabetic subjects without evidence of congestive failure (D'Elia *et al.*)<sup>3</sup>. Several mechanisms for diabetic cardiomyopathy have been proposed including small and microvascular disease, autonomic dysfunction, metabolic derangements, interstitial fibrosis and the development of fibrosis, possibly caused by the accumulation of a periodic acid-Schiff-positive glycoprotein, leading to myocardial hypertrophy and diastolic dysfunction. Growth hormone also appears to be involved in the pathogenesis of angiopathy in the diabetic patients.<sup>4,7</sup>

The present study was done to identify the prevalence of diastolic dysfunction in young asymptomatic diabetics and to analyze whether its prevalence varies with glycemic control and duration of diabetes.

## MATERIAL AND METHODS

The study included 100 young (<40 years with 50 males and 50 females) diabetic patients in Sri Ramachandra Medical College and Hospital from the year 2011 to 2013. 50 healthy controls under 40 years (25 males and 25 females) were taken. A thorough clinical examination was done. All routine lab parameters, fasting and post-prandial sugars, hemoglobin A1c (HbA1c), Chest X-ray, electrocardiogram (ECG), and two-dimensional echocardiogram (2D ECHO) were done for all patients. Diabetic patients aged >40 years, presence of cardiovascular symptoms, hypertensive (more than 140/90 mm of Hg), abnormal resting ECG, patients with positive TMT, smokers, renal failure, signs of vascular involvement (defined as absent peripheral pulses in the lower limb, amputation because of gangrene) and patients with complications of peripheral neuropathy or retinopathy were excluded from the study.

All ECHO recordings and measurements were obtained by the same observer according to the recommendations of the "American Society of Echocardiography" and were always performed at midday to avoid the influence to the circadian rhythm on LVDD. LVDD was evaluated using well-standardized diagnostic criteria and Doppler measurements were done at end expiration. The definitions published by Canadian consensus on diastolic dysfunction by ECHO were used to classify diastolic dysfunction as normal, impaired relaxation, pseudonormal or restrictive pattern. HbA1c was measured by an affinity binding assay.

## RESULTS

Out of 100 young diabetics, 50 males and 50 females were included in the study with 50 healthy controls. The mean age of patients was 29.02 (minimum age 21 years). 30 patients had Type I diabetes. 60 patients had a duration of diabetes less than 6 months (mean duration 3.2 months), 30 patients with duration 6 months-3 years (mean duration 1.33 years), and 10 had duration more than 3 years (mean duration 6.25 years). 60 patients had HbA1c <7, 30 patients with 7-8 and 10 had >8.

Among 60 patients with <6 months duration of diabetes, LVDD was found in 18 patients. Out of 30 patients who had DM of 6 months-3 years duration LVDD was found in 9. Of 10 patients who had DM more than 3 years duration, LVDD was found in 3 patients. Of these 40 patients on

whom HbA1c was done, 70 had good glycemic control and 18 of them had LVDD. 10 had poor glycemic control and 3 of them had LVDD (Table 1).

LVDD was found in 30 patients. All patients had impaired relaxation by ECHO. No patients had pseudonormal pattern or restrictive pattern (Table 2).

## DISCUSSION

In the present study, the overall prevalence of LVDD in young diabetic patients is 30%. The study by Zarich *et al.*<sup>7</sup> revealed the prevalence of diastolic dysfunction was 30% only. The earlier studies pointed out that prevalence was more. In several of these earlier reports, many of these asymptomatic diabetic patients were older or may have had coexistent illnesses known to affect ventricular function. Subsequent studies have focused on younger patients and have excluded subjects at risk for cardiac dysfunction with other comorbidities.

Of the 50 females 20 patients (40%) had LVDD, while 10 out of 56 males had LVDD (20%). In the Framingham Heart study<sup>8</sup> also females outnumbered the males. Among 70 Type II DM patients, 21 had LVDD (30%) while among 30 Type I DM patients 9 had LVDD (30%). In a

study by Raev,<sup>9</sup> diastolic dysfunction was present even in patients of 6 months duration of diabetes. Our results also correlate with this study. This indicates that pre-clinical cardiomyopathy in diabetes has different pathogenesis not related to the duration of DM or glycemic control. Diastolic dysfunction in diabetes must involve the same pathogenetic mechanisms as in any other etiology. This is of great interest and has given rise to many hypothetical mechanisms. Correlation of Diastolic dysfunction and autonomic neuropathy among diabetic subjects revealed that diastolic dysfunction and autonomic neuropathy are both common problems among diabetics.

In a study by Mishra *et al.*,<sup>10</sup> duration of diabetes correlated well with diastolic dysfunction which is in contrary to the present study. Studies by Di Bonito *et al.*<sup>11</sup> and Boyer *et al.*<sup>12</sup> had concluded that diastolic dysfunction occurs early in diabetes. From *et al.*<sup>13</sup> had studied the incidence of early heart failure in diabetic patients with LVDD.

The strength of the study is that it studied a specific group of young diabetics with equal males and females with matched controls, but the limitations remain. Subjects with uncomplicated diabetes are difficult to study because of the high incidence of coexistent CAD and hypertension. In this study, we attempted to rule out ischemia by performing non-invasive, tests, such as symptom-limited exercise ECG, which is shown to be reliable in excluding CAD. Although pre-clinical atherosclerosis may have present, it is highly unlikely that is an important confounding variable in explaining the observer abnormalities in left ventricular diastolic function. This study was limited to a small group of well-characterized patients to avoid too many confounding variables.

## CONCLUSION

Diastolic dysfunction is present even in early stages of diabetes. The prevalence of diastolic dysfunction in diabetes has a female pre-ponderance in the ratio of 2:1. Diastolic dysfunction does not vary with glycemic control, duration of diabetes or type of diabetes. Even though LVDD has been demonstrated to occur very early in this study, routine ECHO evaluation of all DM patients cannot be recommended, but it is useful to screen all DM patients with the ECHO to detect LVDD.

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**Table 1: The study group and profiles**

Parameter	Number	LVDD
Sex		
Male	50	20
Female	50	10
Types		
Type I DM	30	19
Type II DM	70	21
HbA1c		
<7	60	18
7-8	30	9
>8	10	3
Duration of DM		
<6 months	60	18
6 months-3 years	30	9
>3 years	10	3

DM: Diabetes mellitus, LVDD: Left ventricular diastolic dysfunction, HbA1c: Hemoglobin A1c

**Table 2: Transmitral Doppler flow velocity**

Doppler parameter	Normal subjects (N=70)	Impaired relaxation (N=30)
Number of IVRT (ms)	106±17	109±11
E wave (cm/s)	69±11	56±10
A wave (cm/s)	52±9	71±3
E/A	1.34±0.17	0.79±0.07
DT (ms)	189±42	224±51
A wave duration (ms)	129±16	128±25

IVRT: Isovolumetric relaxation time

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# Modified and Simplified Stamey's Procedure for Stress Urinary Incontinence: A Comparative Clinical Study

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## Abstract

**Background:** The purpose of this clinical study was to assess whether a modified and simplified Stamey's procedure for stress urinary incontinence (SUI) has better effects when used for female SUI patients.

**Materials and Methods:** Randomized prospective studies were prepared performed in 30 patients with the SUI percutaneous vesical neck suspension. Technique was similar to advocated by Parra and Shaker (1990) except that no suprapubic catheter was used, and multiple knots were applied and central buttress we have used single stand of proline suture. The results were recorded.

**Results:** There were significant differences in urinary incontinence results. The 28 patients could void without leak. In 2 patients per urethral catheter had to be re-introduced and maintained for 10 days before they could void without retention.

**Conclusion:** Simplification and modification of standard stamey's procedure for stress urinary continence in females is much easy with comparatively better results are achieved.

**Key words:** Incontinence, Proline suture, Stamey's procedure, Stress urinary incontinence

## INTRODUCTION

The definition of stress urinary continence a condition of urine while straining, e.g., during coughing, sneezing, laughing, lifting heavy object, i.e., on raising intra-abdominal pressure.

Most of what we know about urinary continence in the normal female is from what we have learned about stress urinary incontinence (SUI). For this reason, plus the fact that SUI is very common, most of the emphasis in this chapter is on SUI, but the urologist should remember that

much of the information is applicable to patients with total urinary incontinence from widely diverse causes such as pelvic fractures, radiation incontinence, and iatrogenic surgical incontinence.

The percutaneous vesical neck suspension was first introduced by Pereyra but Stamey's established the technique for management of SUI. The original technique has been modified from time to time by various authors (Cobbs and Ragde, Gitte and Loughlin, Parra and Shaker) in attempting to make it similarly and easy.<sup>1-4</sup> We have performed this operation in a modified way. In variance to previous techniques we have used a single proline suture buttress with stay to one side suspension suture which was removed vaginally just by pulling out after voiding. In two cases of retention one side suspension suture was cut vaginally by pulling stay suture.

The aim of the study was to improve and compare by modification and simplification standard Stamey's

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procedure by not using suprapubic catheter and using single strand of proline and stay to the suspension suture.

## MATERIALS AND METHODS

The protocol was approved by the local Ethics Committee and written informed consent was obtained from each patient. A total 30 patients of stress incontinence have undergone this procedure after thorough evaluation. Their age ranged from 28 to 60 years. 25 patients developed stress incontinence in post-menopausal period, 3 following hysterectomy and 2 had their symptoms following delivery. Of 30 patients, 2 had Grade I, 23 Grade II and 5 had grade stress incontinence. Uterine prolapse cases were not included in this study. Urodynamically, they were evaluated.

### Operative Technique

As a standard technique, the patient is kept in lithotomy position under epidural or spinal anesthesia. A 16 F Foley's catheter is introduced and balloon is inflated. Two small suprapubic incisions are made on each side of midline 1 cm above pubic symphysis. Two Stamey's needles are introduced through one of suprapubic incision at a distance of 1 cm from each other and brought out lateral to bladder neck into vagina. Traction on Foley's catheter and finger palpation aids in recognizing and guiding the tip of the needle. The Foley's catheter is now removed and cystoscopy is performed to see that the needles are not passing through the lumen or the wall of bladder.<sup>5,6</sup>

In the center of number I proline suture 9-10 knots are made as shown in Figure 1. The ends of proline suture are threaded through two Stameys needles, which are similar procedure, are performed on the other side. The bladder is now distended with saline till urine leaks out. Both the sutures are pulled up till the leak stops even on putting pressure over the bladder suprapubically. Cystoscopic examination is performed before tying the sutures to see that the bladder neck is closed and if found satisfactory, the sutures are tied Figure 2. On one side of suspension suture a mersilk thread is put vaginally with loose knot. On 3<sup>rd</sup> post-operative day catheter is removed and voiding trial is given. Vaginally mersilk is just pulled out if she voids normally.

## RESULTS

All the patients withstood the operation well without any immediate post-operative complications. Out of 30, 28 patients could void without leak. 2 patients could not void in immediate post-operative period per urethra catheter was put for 10-day. Subsequently, they also voided without leak. One patient there was retention and vaginal sling thread was pulled and suspension suture of one side was just cut and

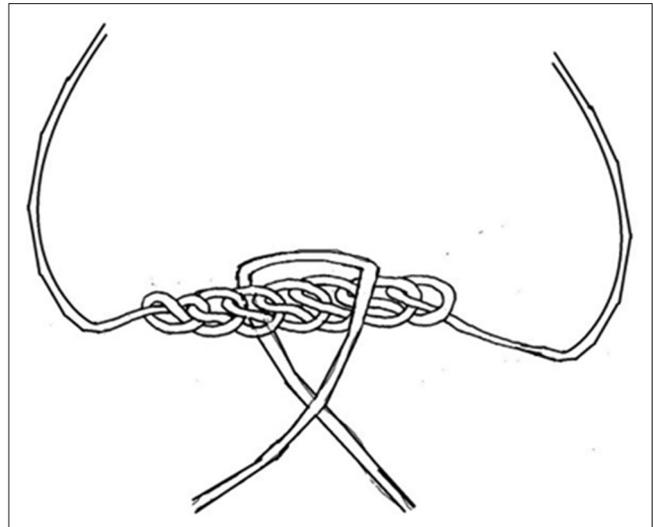


Figure 1: Central buttress suture with vaginal knot



Figure 2: Stamey's suture before being tied with vaginal sling

later she voided well. Delayed recurrence was seen in one patient. She presented with leak after 1-year.<sup>7-9</sup>

Table 1 depicts grading of cases of present study as given by Ingelman-Sundberg.

Clinical grading (Ingelman-Sundberg):

- Grade I: When leakage or urine occurs on straining
- Grade II: When incontinence occurs following abrupt movement
- Grade III: When leakage occurs on just getting up from bed or even in lying position in bed.

Clinical features like leakage of urine is the sole presentation, leakage on stress, Bonney's test, associate prolapsed are presented in Table 2.

Complications are presented in Table 3 like wound infection suprapubic, retention of urine, urinary incontinence.

**Table 1: Grading of cases**

Grade	Cases
I	2
II	23
III	5

**Table 2: Clinical features**

Clinical assessment	Number of cases
Leakage of urine is the sole presentation	8 cases
Leakage on stress	22 cases
Bonney's test	Positive
Associate prolapsed	Not included

**Table 3: Complications**

Post operative complication	No: of cases
Wound infection suprapubic	1 case diabetic - anti-biotics given
Retention of urine	2 cases
Urinary incontinence	1 case after 1-year

## DISCUSSION

The results of present study demonstrated that the modifications and simplification of procedure are excellent and a control stay on suspension suture on one side. The results are reproducible.

### Advantages and Comparison with Other Methods

In classical Stamey's procedure vaginal incision is given and Dacron or Gortex buttress is used for pubovaginal suspension. Gittes and Loughlin modified the technique advocating no vaginal incision and instead of Dacron buttress they took 3-4 bite through vaginal wall.

Parra and Shaker further modified the procedure and their technique was same as Gittes and Loughlin except instead of vaginal suture, they advocated double barrel knot. It requires two stands of proline sutures and cut ends of each remains inside the vagina. We have further modified and used single stand of proline suture with buttress made in the center with specially designed knots which is much easier to make. There is no fear of slippage of ligature which is a possibility in Parra and Shaker technique as well as there are no free cut ends of proline sutures in the vagina which may be troublesome to the patients.<sup>5,10,11</sup>

In our method, we have applied vaginal sling to suspension suture of one side so that in case of retention one side can be cut. This helps in controlling or cutting suspension suture if it is very tight. Without this suspension thread it is very difficult to cut the vaginal sling, in lithotomy position and no anesthesia is required.

In SUI, the suspension of bladder neck by proline suture works by incorporation of suture into tissue and subsequent fibrous band formation on either side of the bladder neck. We have used a centrally knotted single strand of proline suture that would act as a buttress support in pulling the bladder neck when suture will be tied. We have used single Stamey's needle punctured twice suprapubically with 1 cm spacing. We have used vaginal sling for cutting bladder neck suspension suture in case there is retention. Our results with this technique are comparable with others.

## CONCLUSION

On the basis of our current study modification and simplifications has an advantage over standard Stamey's suspension for female stress incontinence in cases.

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# Creatinine Clearance by Timed Urine Collection for Measurement of Glomerular Filtration Rate in Liver Cirrhosis: A Feasible Method

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## Abstract

**Background:** Renal dysfunction is one of the common and major complications in liver cirrhosis with poor prognosis.

**Aim:** To study the role of serum creatinine and creatinine clearance in assessing renal function in patients with liver cirrhosis and to study the advantages of measuring the creatinine clearance by timed urine collection over creatinine clearance measured by Cockcroft-Gault formula.

**Materials and Methods:** All adult patients of both sexes diagnosed to have liver cirrhosis were included in the study. Liver function test, renal function tests, 24-h urine volume, and urine creatinine were done. Creatinine clearance was calculated using the formula urine creatinine/serum creatinine multiplied by 24-h urine volume and also by the Cockcroft-Gault formula. Comparison between serum creatinine and creatinine clearance calculated by these two methods were done.

**Results:** Of the 43 patients included in the study, 35 were male while remaining 8 were female. Mean blood urea and serum creatinine were 22.42 mg/dl and 1.01 mg/dl. 10 patients had a creatinine clearance of <30 ml/min based on timed urine collection. Measurement of creatinine clearance using the Cockcroft-Gault formula showed significantly higher values when compared to that measured using timed urine collection. Ascites was present in 38 out of the 43 patients. Kidney size and corticomedullary differentiation were normal in all patients.

**Conclusion:** Creatinine clearance should be done routinely in advanced liver disease to assess renal reserve. Creatinine clearance by timed urine collection has a strong predictive value when compared to creatinine clearance done using by Cockcroft-Gault formula.

**Key words:** Cockcroft-Gault formula, Glomerular filtration rate, Liver cirrhosis, Timed urine creatinine clearance

## INTRODUCTION

Renal dysfunction is one of the common and major complication in liver cirrhosis with poor prognosis.<sup>1,2</sup> Assessment of renal function is important to monitor the progression of renal disease in liver cirrhosis.<sup>1</sup> Most widely used standard methods to assess renal function like blood urea nitrogen, serum creatinine are likely to give erroneous

impressions in liver cirrhosis.<sup>3</sup> Accurate measurement of glomerular filtration rate requires use of a validated filtration marker, such as iothalamate, iothexol, or inulin.<sup>2</sup> Inulin clearance is the gold standard for measurement of glomerular filtration rate.<sup>4,6</sup> However, the applicability of these markers is restricted by its cost and feasibility and is rarely used in clinical practice.<sup>4</sup> Here, we have studied the advantages of using a more practically feasible marker of glomerular filtration rate, the creatinine clearance to assess the renal function in routine clinical practice.

## MATERIALS AND METHODS

In Present, Study was carried out in Aarupadaai Veedu Medical College and Hospital, Pondicherry, India during

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the period of October 2012 to September 2015. All adult patients of both sexes diagnosed to have liver cirrhosis were included in the study. As glomerular filtration rate decreases with age,<sup>6,7</sup> patients of age more than 60 years were excluded from the study. Patients with chronic kidney disease, primary renal disease, diabetes mellitus, systemic hypertension, serum creatinine >1.5, hepatic encephalopathy, recent gastrointestinal bleed were also excluded from the study. Laboratory investigations liver function test, renal function tests, serological tests for hepatitis virus B and C, 24-h urine volume, and urine creatinine was done. Ultrasonogram of the abdomen was done to identify the liver size, echotexture, portal vein diameter, splenomegaly, presence of ascites and kidney size, echotexture. Evidence of liver cirrhosis was defined by a compatible clinical profile<sup>8,9</sup> along with altered liver function tests, reversal of albumin-globulin ratio, shrunken liver with altered echotexture in ultrasonogram. Creatinine clearance calculation was done by two methods, one by timed urine collection<sup>10</sup> using the formula urine creatinine/serum creatinine multiplied by 24-h urine volume (UCr/PCr) × V. This was divided by 1440 to get the value in ml/min. The patients were sub-grouped into three based on their creatinine clearance using (U×V)/P. Group I having values more than 60 ml/min, Group II 30-60 ml/min and Group III <30 ml/min. Creatinine clearance was also calculated using the Cockcroft and Gault formula<sup>10</sup> (140-age)×weight/(serum creatinine×72). For female patients this value to be multiplied by 0.85. Comparison between serum creatinine and creatinine clearance calculated by these two methods were done.

## RESULTS

Of the 43 patients included in the study, 35 were male and 8 were female. Age of the patients ranged from 22 to 58 years (Table 1). The mean age was 42.14 years. The liver disease was associated with alcoholism in 21 patients, hepatitis B virus in 6 patients, Wilson's disease in one and autoimmune hepatitis in one patient. In the remaining 14 patients, etiology could not be ascertained. A number of patients with creatinine clearance <30 ml/min based on timed urine collection was 10 (Table 2). Mean blood urea level was 22.42 mg/dl. The serum creatinine was 0.90 mg/dl Group I patients (Table 3) and the mean serum creatinine level was 1.01 mg/dl. The 24-h urine volume in Group III patients was 690 ml, and the mean 24-h urine volume was 1317.44 ml. Measurement of creatinine clearance using the Cockcroft-Gault formula showed significantly higher values when compared to that measured using timed urine collection (Table 4). Mean serum albumin was 3.37 mg/dl (Table 5). The mean

**Table 1: Age and number of patients**

Age group (years)	Number of patients
<30	2
30-39	9
40-49	24
50-60	8

**Table 2: Number of patients and creatinine clearance by timed urine collection**

Group	Creatinine clearance (ml/min)	Number of patients
Group I	>60	14
Group II	30-60	19
Group III	<30	10

**Table 3: Renal parameters across three groups**

Renal parameter	Group I	Group II	Group III
Blood urea (mg/dl)	22.43	22.42	22.4
Serum creatinine (mg/dl)	0.90	1	1.2
24-h urine volume (ml)	2010.71	1136.84	690
Creatinine clearance (UxV/P) ml/min	85.33	43.41	18.55
Creatinine clearance (CG formula) ml/min	85.02	63.87	44.90

**Table 4: Comparison of creatinine clearance by two methods**

Creatinine clearance (ml/min)	By (U×V)/P (%)	By Cockcroft Gault formula (%)
<20	6 (13.95)	0 (0)
20-40	12 (27.90)	4 (9.30)
40-60	11 (25.58)	11 (25.58)
60-80	5 (11.63)	17 (39.54)
>80	9 (20.93)	11 (25.58)

**Table 5: Serum albumin and renal function**

Serum albumin (mg/dl)	Group I	Group II	Group III
>3.5	8	2	0
3.2-3.5	4	14	3
<3.2	2	3	7

**Table 6: Serum bilirubin and renal function**

Serum bilirubin (mg/dl)	Group I	Group II	Group III
<1.2	2	2	3
1.2-2	8	12	4
>2	4	5	3

bilirubin was 1.64 mg/dl (Table 6). Ultrasound abdomen showed shrunken liver with altered echotexture and splenomegaly in all the patients. Ascites was present in 38 out of the 43 patients. Kidney size and corticomedullary differentiation were normal in all patients.

## DISCUSSION

Of the total 43 patients included in the present study with liver cirrhosis, male (81%) patients were more common than female (19%) patients. Most common age group (Table 1) of presentation with liver cirrhosis in the present study was 40-49 years with 24 (56%) patients. Alcoholism was the commonest cause of liver disease in the present study with 21 (49%) patients, followed by hepatitis B in 6 (14%) patients. In our study, there was no significant variation in blood urea levels (Table 3) in all the three groups, suggesting that estimation of blood urea will not be of much use in determining renal impairment. Blood urea nitrogen levels may also vary in the absence of glomerular filtration rate changes as blood urea levels may be lower than expected in patients with liver disease because of reduced hepatic synthesis, and it may also increase because of gastrointestinal hemorrhage or catabolic states.<sup>11</sup> Hence, its use to assess renal dysfunction is very limited. It was noted that in 10 patients with normal serum creatinine levels below 1.2 mg/dl, the creatinine clearance was less than 30 ml/min (Table 2) of, suggesting that moderate to severe renal dysfunction may be masked by seemingly normal creatinine levels.<sup>13</sup> This is possibly due to the fact that the hepatic production of creatinine is impaired in cirrhosis<sup>13,14</sup> and the presence of malnutrition, increased tubular secretion in cirrhosis further reduce the serum creatinine level and decrease the accuracy of serum creatinine in assessing the renal function in cirrhosis liver.<sup>1</sup> Patients with cirrhosis and serum creatinine above 1.5 mg/dl have a glomerular filtration rate below 30 ml/min.<sup>9</sup> Hence, patients with creatinine levels >1.5 mg/dl were excluded from our study. The present study showed that serum creatinine alone in patients with the advanced liver disease is of limited value for identification of renal dysfunction. This is in agreement with the findings in a study by MacAulay *et al.*<sup>12</sup> Another prospective study of a large number of cirrhotic patients by Papadakis and Arieff<sup>13</sup> also indicated that the glomerular filtration rate can be very low, even when the serum creatinine is <1.0 mg/dl. In our study, patients with greater degrees of renal impairment were found to have lesser urine output, thus suggesting that eliciting history of oliguria in a cirrhotic patient with normal serum creatinine level should call for a high index of suspicion of renal dysfunction. Serum albumin (Table 5) was found to have a direct correlation with renal function,<sup>15</sup> patients with higher creatinine clearance level were seen to have higher serum albumin levels. Serum bilirubin (Table 6) did not show any direct correlation with renal function.<sup>19</sup> Except for the five patients belonging to Group I with creatinine clearance >60 ml/min, all other (88%) patients had ascites, though their serum creatinine was normal thus suggesting that presence of ascites may be one of the first changes

of worsening renal function.<sup>19</sup> The present study showed that patients with alcoholic liver disease<sup>5</sup> were predisposed to develop renal impairment when compared with liver disease of other etiologies. Only 20% of alcoholic patients had a creatinine clearance of >60 ml/min as compared to 50% of cirrhotic patients due to hepatitis B. Present study, also showed calculating creatinine clearance by Cockcroft-Gault formula (Table 4) overestimates renal function. This is probably due to discrepancies in weight due to fluid retention which is one of the consequences of renal impairment in cirrhotics. As weight is one of the variables in the numerator of the formula, an increase in weight due to edema or ascites will give a spuriously high creatinine clearance. The study by MacAulay *et al.* also supports this finding.<sup>12</sup> This overestimation of renal function was highest in patients with lower glomerular filtration rate, which was observed in present Study also. Inulin clearance<sup>2</sup> along with other more accurate methods like radioisotopes <sup>99m</sup>Tc-DTPA, <sup>169</sup>Yb-DTPA, or <sup>125</sup>I-iothalamate to estimate glomerular filtration rate is not feasible in routine clinical practice because of the complexity, cost, and limited availability.<sup>4,6</sup> MacAulay *et al.*<sup>12</sup> observed that among the creatinine-based glomerular filtration rate formulas, the MDRD formula developed by the modification of diet in renal disease (MDRD) study group is the best formula for detection of moderate renal dysfunction among those with cirrhosis. Francoz *et al.*,<sup>16</sup> in their study have observed that MDRD which does not take into account the body weight seems to be less inaccurate than Cockcroft in cirrhotic patient. However, they also observed that the accuracy of MDRD, even if slightly superior to that of Cockcroft, remains limited. Eren and Kantarci<sup>2</sup> in their study have observed that all these equations have been validated in patients with end-stage renal disease<sup>17</sup> and in renal transplant recipients,<sup>18</sup> but they have not been validated in either the cirrhotic or the post-liver transplant population. As MDRD formula requires web-based calculations, it will be impractical to rely on it as a parameter of assessing renal function in a resource limited setup. However, the above-mentioned studies did not include any formulas requiring urine collection. Measured creatinine clearance from timed urine collections is a relatively inexpensive, accessible method used in clinical practice. In present Study measurement of creatinine clearance using Cockcroft Gault formula showed significantly higher values, suggesting overestimation in measurement of glomerular filtration rate. Five out of the 28 patients (18%) with creatinine clearance >60 ml/min by Cockcroft-Gault formula were found to have creatinine clearance values <40 ml/min, when calculated by timed urine collection. *P* value calculated was found to be <0.0001, which is statistically significant. Present Study showed that creatinine clearance from timed urine collections provides a better estimate of a renal reserve than serum creatinine or predicted creatinine

clearance by Cockcroft-Gault formula. A systematic review and meta-analysis of patients with cirrhosis by Proulx *et al.*<sup>9</sup> showed that creatinine clearance measured by timed urine collections is a preferable method in clinical practice, as it is more reliable than serum creatinine or creatinine clearance calculated by Cockcroft-Gault formula. Proulx *et al.*<sup>9</sup> also suggested that creatinine clearance was an aid in determining true glomerular filtration rate when inulin clearance was not available or feasible and may be a useful clinical test in the evaluation of renal insufficiency in cirrhotic patients with normal serum creatinine values.

## CONCLUSIONS

Creatinine clearance should be done routinely in all patients with liver cirrhosis to assess renal function, as blood urea and serum creatinine are not reliable markers of renal dysfunction in liver cirrhosis. Creatinine clearance measurement by timed urine collection is a more practically feasible and cost effective method, and it has a strong predictive value when compared to calculating creatinine clearance by Cockcroft-Gault formula in the measurement of glomerular filtration rate to assess the renal function in patients with liver cirrhosis.

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# Platelet Indices in Preterm Neonates: A Prospective Study

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## Abstract

**Introduction:** Platelets in neonates are necessary for hemostasis, phagocytosis, and for maintaining blood vessel integrity. Physiological status of newborn affects hemostatic mechanism. Prematurity, birth asphyxia, and small for gestational age babies are associated with hemostatic abnormalities. The aim of this study was to compare blood platelet indices in preterm neonates and full-term appropriate for gestational age (AGA) neonates and to check whether prematurity affects platelet indices or not.

**Materials and Methods:** Present study was a prospective study conducted in the neonatal intensive care unit of a tertiary care teaching hospital. 30 preterm neonates and an equal number of full-term AGA neonates were included, blood samples were collected within 24 h of birth, and platelet indices were estimated. The data thus obtained was analyzed using the appropriate statistical tool.

**Results:** Sex distribution among both groups was identical. The ratio of male to females in the study was 1.4:1. Mean platelet count in preterm neonates ( $219.72 \times 10^3/\text{mm}^3$ ) was low as compared to term neonates ( $251.26 \times 10^3/\text{mm}^3$ ),  $P = 0.002$ . Plateletcrit (PCT) was also decreased in preterm neonates as compared to term neonates (0.19% vs. 0.21%),  $P = 0.016$ . Mean platelet volume was found to be similar in both preterm and term neonates (8.12 fl and 7.95 fl respectively). Platelet distribution width (PDW) was higher in preterm neonates (15.75) as compared to that of term neonates (12.89).

**Conclusion:** Low values of platelet counts, PCT, and increase in PDW seen in preterm neonates may be due to low gestational age and weight or due to dysfunction of megakaryocytes. Platelet indices may be a vital marker for identification of hemostatic disorders in newborns.

**Key words:** Mean platelet volume, Prematurity, Platelet count, Plateletcrit, Platelet distribution width

## INTRODUCTION

With the improvement in the perinatal and neonatal care, there has been a significant reduction in neonatal mortality and has helped in improvement in survival of preterm neonates.<sup>1</sup> Platelets in neonates are necessary for hemostasis, for maintaining blood vessel integrity and phagocytosis. Hemostasis in a neonate is a dynamic entity which evolves gradually throughout the fetal period and early infancy.<sup>2</sup> Physiological status of newborn affects the hemostasis mechanism. Prematurity, birth asphyxia and

small for gestational age babies (SGA) are associated with hemostatic abnormalities.<sup>3,4</sup>

Hemostasis in newborns is less efficient in comparison to adults.<sup>5</sup> In preterm neonates, blood platelet count is observed to be decreased, depending on the birth weight and gestational age.<sup>6</sup> Platelet has an important role in initiating the thrombotic event, but platelet count alone does not give a complete picture of platelet maturity and its function. Platelet indices such as mean platelet volume (MPV), plateletcrit (PCT), and platelet distribution width (PDW) are utilized for this purpose. Platelet size can be analyzed using MPV and PDW, and it correlates with the activity of platelets. Large platelets are more active and have high thrombotic potential. Hence, these parameters can be used to diagnose thromboembolic disorders at the earliest.

Around 18-35% of neonates admitted to neonatal intensive care unit (NICU) are found to have a platelet

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count of  $\leq 150,000$  cells/ $\mu\text{l}$  at some point of time during stay in NICU.<sup>7-9</sup> It has been observed that the risk of thrombocytopenia in NICU is high among preterm neonates, and it is highest among the most preterm infants.<sup>10</sup> Preterm neonates are prone to develop various complications like intraventricular hemorrhage, chronic lung disease. It has been observed that platelet indices can be used to predict the development of above-mentioned complications at an early stage.<sup>11,12</sup> Only a few studies have been done to determine platelet indices in preterm neonates. The aim of this study was to determine platelet indices in preterm neonates and to compare it with full-term appropriate for gestational age (AGA) healthy neonates. The main focus of this study was to check whether prematurity affects platelet indices or not.

## MATERIALS AND METHODS

The present study was a prospective study conducted in NICU, Department of Pediatrics, Mandya Institute of Medical Sciences, Mandya, Karnataka, India. The study was conducted during July-August 2015. The study consisted of 60 newborns whose blood samples were collected in K<sub>2</sub> ethylenediaminetetraacetic acid tubes within 24 h of birth for complete blood counts. Samples were analyzed using hematology auto analyzer. The following parameters were studied-platelet count, MPV, PCT, PDW. A platelet count of  $\leq 150,000/\mu\text{l}$  was used to define thrombocytopenia. Samples obtained from neonates after 24 h of birth or neonates with birth asphyxia, clinically or laboratory-confirmed infections, major congenital anomalies were excluded from the study.

Neonates were included into the study after obtaining informed written consent from parents. Detailed history regarding antenatal checkup in mother, mode of delivery was obtained. Data regarding the neonatal physiological status with respect to prematurity and gestational age were collected. Both groups of newborns and their mothers were free of infections. There was no pregnancy and perinatal complications. No drugs affecting the functions of platelets were administered to mothers within 10 days before delivery. They were subjected for thorough physical examination. Gestational age was calculated from the date of last menstrual period, in concordance with New Ballard Score.<sup>13</sup> Newborns in gestational age 25-34 weeks and weighing 1000-2150 g with Apgar score of 4-8 at 1 min were considered as preterm neonates. Newborns of gestational age 37-42 weeks and weighing 2500-3900 g with Apgar score of 8-10 at 1 min were considered as full-term AGA neonates.

The data collected were entered in MS Excel spreadsheet. The results are expressed as mean  $\pm$  standard deviation.

Observations were statistically analyzed using Epi Info software version 3.5.1. The Mann-Whitney *U* test was used to analyze the relationship between the two groups. A  $P < 0.05$  was considered as statistically significant. Descriptive statistics was applied for non-parametric data. This study was approved by Institutional Ethics Committee.

## RESULTS

A total of 60 newborns delivered during the study period were included in the present study, of which 30 were full-term AGA neonates and rest 30 were preterm neonates. Out of 60 newborns 58.33% (35) male and 41.67% (25) were females, ratio is 1.4:1. The sex distribution among the study groups was identical (Table 1).

The characteristics of newborns included in the study are shown in Table 2. Mean gestational age in full-term AGA group was 38.87 weeks and in preterm group was 31.71 weeks. Mean birth weight in full-term AGA group was 2937.33 g and in preterm group was 1572.47 g. Mean length in full-term AGA group was 48.89 cm and in preterm group was 40.24 cm. Mean head circumference in full-term AGA group was 34.56 cm and in preterm group was 28.73 cm.

Blood investigation values of study subject are depicted in Table 3. Mean hemoglobin in term neonates was  $16.58 \pm 2.09$  (g/dl) as compared to  $18.19 \pm 1.83$  (g/dl) of preterm neonates, and the difference was statistically significant ( $P = 0.002$ ). Platelet counts in preterm neonates were lower in comparison to term neonates ( $219.72 \times 10^3/\text{mm}^3$  vs  $251.26 \times 10^3/\text{mm}^3$ ), and the difference was statistically significant ( $P = 0.016$ ). PCT

**Table 1: Sex distribution of study subjects**

Sex	Full-term AGA newborns (%)	Preterm newborns (%)	Total (%)
Male	17 (56.67)	18 (60)	35 (58.33)
Female	13 (43.33)	12 (40)	25 (41.67)
Total	30 (50)	30 (50)	60 (100)

AGA: Appropriate for gestational age

**Table 2: Gestational age and anthropometric characteristics of study infants**

Parameter	Mean (range) (n=30)	
	Full-term AGA newborns	Preterm newborns
Gestational age (weeks)	38.87 (37.14-41.29)	31.71 (28.14-33.86)
Birth weight (g)	2937.33 (2650-3870)	1572.47 (1060-2120)
Length (cm)	48.89 (45.7-53.2)	40.24 (34-46.1)
Head circumference (cm)	34.56 (33.1-35.9)	28.73 (24.3-32)

AGA: Appropriate for gestational age

**Table 3: Hemoglobin and blood platelet indices in study infants**

Parameter	Mean±SD		P value
	Full-term AGA newborns	Preterm newborns	
Hemoglobin (g/dl)	16.58±2.09	18.19±1.83	0.002
Platelet count ( $\times 10^3/\text{mm}^3$ )	251.26±63.34	219.72±65.91	0.016
PCT (%)	0.21±0.04	0.19±0.05	0.026
MPV (fl)	7.95±0.60	8.12±0.64	0.247
PDW	12.89±4.65	15.75±6.41	0.029

AGA: Appropriate for gestational age, PCT: Plateletcrit, MPV: Mean platelet volume, PDW: Platelet distribution width, SD: Standard deviation

was also low in preterm neonates as compared to term neonates (0.19% vs. 0.21%), the difference in observation was statistically significant ( $P = 0.026$ ). MPV was similar in both preterm and term neonates (8.12 fl vs. 7.95 fl) ( $P = 0.247$ ). PDW or platelet anisocytosis index was more in preterm neonates (15.75) as compared to term neonates (12.89), and the variation was statistically significant ( $P = 0.029$ ).

## DISCUSSION

Hemostasis in a neonate is a dynamic entity which evolves gradually throughout the fetal and early infancy. Platelets first appear in human fetus at the gestational age of 5 weeks postconception, it gradually increases during the fetal life to reach the adult value by gestational age of 22 weeks.<sup>2</sup> Prematurity, birth asphyxia, and SGA babies are associated with hemostatic abnormalities.<sup>3-6</sup> Hence preterm neonates are at higher risk of hemorrhagic and thrombotic complications, which leads to increase the morbidity and mortality in the preterm neonates.

In our study, it was observed that mean hemoglobin levels in preterm neonates were more as compared to that of term neonates. Polycythemia is a commonly expected problem in preterm neonates.<sup>14</sup> This study showed that average number of platelets in preterm was significantly lower than the platelet count of term neonates. In our study, PCT was lower in preterm neonates in comparison to term neonates, and the difference was statistically significant. In studies by Wasiluk *et al.*, Kannar *et al.* have also reported that platelet counts and PCT in preterm neonate are low in comparison to term neonates.<sup>15,16</sup>

MPV is the measurement of the average size of the platelet in blood and PDW reflects the variation of platelet size. In the present study, MPV was found to be slightly higher in preterm neonates in comparison to term neonates but the difference was not statistically significant. PDW was found to be significantly higher in preterm neonates as compared

to term neonates. Similar findings have been reported in study done by Wasiluk *et al.*<sup>15</sup> However, in study done by Kannar *et al.* have reported that MPV is significantly elevated in preterm neonates.<sup>16</sup>

Lower platelet counts observed in preterm neonates is mostly due to developmental limitation in the ability to increase megakaryocyte size and placental dysfunction may also be responsible for the alteration of platelet count in newborns at birth.<sup>17,18</sup> The reduced platelet count and their function in relation to gestational age may result in higher risk of bleeding tendency in preterm neonates.<sup>4</sup> Elevated PDW without much alteration in MPV may indicate that PDW is a more sensitive index for estimation of changes in platelet size.<sup>19,20</sup> Increase in PDW may be due to negative correlation with gestational age and birth weight.<sup>19</sup> PDW may be useful in detection of conditions like sepsis, platelet consumption at an early stage.<sup>21</sup> The increase in MPV is seen in conditions like disseminated intravascular coagulation which is associated with platelet activation and consumption. Platelet indices determined by automated hematological analyzers may be very useful tool in the diagnosis of hemostatic disorders and infections, which are more often found in preterm newborns.

## CONCLUSION

Low values of platelet counts, PCT, and increase in PDW seen in preterm neonates may be due to low gestational age and weight or due to dysfunction of megakaryocytes. Platelet indices may be a vital marker for identification of hemostatic disorders in newborns.

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# Serum Magnesium Levels in Critically Ill Patients: A Prospective Study

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## Abstract

**Background:** Though the importance of magnesium is known, it is not a usually recognized electrolyte abnormality in clinical practice. The prevalence of hypomagnesemia may be high in critically ill patients.

**Materials and Methods:** It was a prospective, observational study. A total of 150 consecutive critically ill patients admitted to the intensive care units of JSS Hospital, Mysore under the Department of General Medicine fulfilling inclusion and exclusion criteria were studied. Serum magnesium levels along with other relevant investigations were done within first 24 h of hospital admission. The hospitalization details and progress of the patients were recorded. Patients were followed up until the end points, i.e., discharge by the treating physician, discharge against medical advice or in-hospital death, and discharge for a referral.

**Results:** On admission 94 out of 150 (i.e., 63%) had normomagnesemia, 45 out of 150 patients (i.e., 30%) had hypomagnesemia, 11 out of 150 (i.e., 7%) had hypermagnesemia. The patients with hypomagnesemia “compared with” patients with normomagnesemia, had higher mortality rate (51% vs. 36%), higher APACHE II score on admission (24.13 vs. 22.47), need of ventilator support was more frequent (35% vs. 17%), a more frequent hypocalcemia (49% vs. 31%), a more frequent hypoalbuminemia (62% vs. 51%), and a more frequent septicemia (47% vs. 21%). Patients with diabetes (49% vs. 21%), hypertension (53% vs. 30%), and alcoholics (33% vs. 19%) had hypomagnesemia more frequently. There was no association of hypomagnesemia with arrhythmia, neurological manifestations, duration of stay, potassium disturbances, other electrolyte abnormalities creatinine levels, metabolic acidosis, inotropic use type of diet and anemia.

**Conclusion:** This study highlights the magnitude of hypomagnesemia in critically ill patients. Hypomagnesemia was associated with a higher APACHE II score on admission, increased mortality, increased need of ventilator support, hypocalcemia, hypoalbuminemia, and septicemia. There was an association of hypomagnesemia with diabetes and hypertension.

**Key words:** Critical illness, Hypomagnesemia, Magnesium

## INTRODUCTION

Magnesium being the fourth most populous cation in the human body, and the second most populous intracellular cation next to potassium; it plays an essential physiological role in many functions of the body.<sup>1</sup> Hypomagnesemia may have serious implications in critically ill patients.<sup>2</sup>

Magnesium deficiency has a dubious credit of being the most unrecognized electrolyte disorder in routine clinical practice.<sup>3</sup> Though the importance of magnesium has been observed in ill patients, magnesium has been dubbed as the “forgotten cation.”<sup>4,5</sup> Hence, we set out with an objective of studying serum magnesium levels in critically ill patients. This study was conducted over a period of 2-years in a teaching tertiary care referral hospital at Mysore, Karnataka state, South India.

## METHODOLOGY

It was a prospective observational study (descriptive non-interventional study). Institutional Ethics Committee

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Approval was obtained. APACHE score was calculated for each patient on the day of admission to intensive care unit (ICU) using APACHE II scoring system. Critically ill adult patients above the age of 18 years admitted in ICUs with APACHE II score of 18 or more were included. The study included 150 patients admitted in ICUs under the Department of General Internal Medicine over a period of 2-years. Written Informed consent was obtained for all cases. Patients were excluded from the study; if they had received blood products, magnesium or calcium infusions before sampling. Inclusion in the study would not affect the routine patient care in the ICU. Serum Magnesium levels within the first 24 h of admission into the ICU were taken. Samples of venous blood (4.5 ml) were collected from every patient within the first 24 h of admission. Serum magnesium levels were assayed in JSS hospital laboratory by xylydyl blue colorimetric method using IMOLA auto analyzer with the normal range of serum magnesium being 1.7-2.7 mg/dL. The following data were noted: Age, gender, presenting symptoms and signs, diagnosis, relevant investigation reports, treatment and intravenous fluids used, duration of stay in ICU and any complications thereof, any new developments in ICU, use of mechanical ventilation, and its duration and mortality in the ICU, etc. Patients were followed up until discharge (from ICU) or death. All the patients enrolled were studied considering the following parameters: Length of stay in ICU, need for ventilator support, duration of ventilator support, APACHE score and mortality.

### Statistical Methods

Quantitative data is represented as mean  $\pm$  standard deviation. To assess the association among variables the Chi-square test, *t*-test, ANOVA were used. Differences were considered statistically significant if  $P < 0.05$ . Statistical analysis was performed using SPSS version 16.0 for Microsoft windows.

## RESULTS

Out of the total 150 patients, a total of 93 patients were males and 57 were females. Out of total 150 patients 94 patients, i.e., 62.66% had normomagnesium, 45 patients, i.e., 30% of total cases had hypomagnesium (Figure 1). The lowest serum magnesium value was 1.0 mg/dL, and the highest was 4.2 mg/dL with mean being 2.018 mg/dL. Out of total 150 cases, cases with hypermagnesium were only 11, i.e., 7.33% and statistically not significant. Hence, hypermagnesium is not included in the discussion henceforth. Out of the total 45 patients with hypomagnesium, a total of 29 patients were males and 16 were females. In total 150 critically ill cases the mean APACHE II score was  $22.97 \pm 4.06$ , mean

APACHE II score in patients recovered and discharged was  $21.13 \pm 2.88$ , in those who died  $25.00 \pm 4.50$ , in discharged against medical advice  $22.84 \pm 3.17$ , in discharged at request cases  $19.00 \pm 1.41$ , in hypomagnesium cases  $24.13 \pm 4.14$ , in hypomagnesium cases with death as outcome  $25.91 \pm 3.82$ , in hypermagnesium cases  $25.82 \pm 12.24$ . Hypomagnesium was associated with increased mortality and a higher APACHE II score ( $P = 0.02$ ) (Figure 2). The range of duration of stay in critical care unit varied from 1 to 36 days with mean of 7.90 days. The mean duration of stay of patients with low serum magnesium was  $7.15 \pm 6.04$  days in ICUs while that of patients with normal serum magnesium was  $8.31 \pm 7.72$  days and that of patients with high serum magnesium was  $7.45 \pm 5.97$  days. The difference was not statistically significant ( $P > 0.65$ ). Out of total 150 patients 21.33% (32 out of 150) needed ventilator support. 35.5% (16 out of 45) patients with hypomagnesium needed mechanical ventilator support, while only 10.66% (16 out of 94) of the normomagnesium group needed ventilatory support and no patients of hypermagnesium needed ventilator support. Hypomagnesium was associated with increased ventilator requirement ( $P < 0.009$ ). Hypomagnesium was associated with increased incidence of hypocalcemia ( $P = 0.031$ ). There was no significant association between hypomagnesium and other electrolytes (both potassium and sodium). There was a significant association of hypomagnesium with hypoalbuminemia ( $P = 0.03$ ). There was an association between sepsis and hypomagnesium ( $P = 0.015$ ). There was an association between hypomagnesium in critically ill patients and diabetes and/or hypertension. The present study does not show any relation of hypomagnesium with inotropic use, increased creatinine values, presence of metabolic acidosis or anemia. There was an increasing trend of alcoholics having hypomagnesium, even though it was not statistically significant ( $P = 0.08$ ). There was no association of hypomagnesium with arrhythmia or neurological complications. There was no association of hypomagnesium with either diet or smoking.

## DISCUSSION

Hypomagnesium is a common finding in critically ill patients. The prevalence of hypomagnesium in critically ill patients in different studies range from 20% to 65%.<sup>4,13</sup> In the present study, 30% of the patients had hypomagnesium. The majority of the studies done earlier as well as the present study have made use of only total serum magnesium levels, whereas ionized magnesium levels should be measured ideally which gives a better idea of associations since it is the ionized magnesium which is metabolically active.<sup>11</sup> Hypermagnesium is less common compared to hypomagnesium, ranging

from 4% to 14% in different studies.<sup>4-13</sup> In the present study, 7.33% of patients had hypermagneseemia. The association between hypomagneseemia and mortality varies between different studies.<sup>4-13</sup> A higher mortality rate was detected in hypomagneseemic patients as compared to normomagneseemic patients by Chernow *et al.*<sup>5</sup> (41% vs. 13%), Rubeiz *et al.*<sup>7</sup> (46% vs. 25%), Safavi and Honarmand.<sup>12</sup> (55% vs. 35%), and Limaye *et al.*<sup>13</sup> (57.7% vs. 31.7%). Guérin *et al.*<sup>8</sup> had found no difference in mortality in ICU patients between hypomagneseemic and normomagneseemic groups (18% vs. 17%); In the current study, the mortality rate in hypomagneseemic group was 51.1% (Figure 3) which is significantly higher as compared to 36.2% in the normomagneseemic group and 27.3% in the hypermagneseemic group. Whether this increased mortality is due to hypomagneseemia or due to a combination of other electrolyte abnormalities like hypocalcemia, hypoalbuminemia, increased incidence of septicemia, and more risk factors such as diabetes and hypertension or due to the severity of the underlying illness itself is difficult to ascertain. In this study, there is an increased mean APACHE II score in hypomagneseemia and hypermagneseemia group compared with normomagneseemia with a mean of 24.13 in hypomagneseemia group and 22.97 in normomagneseemia group. It shows that hypomagneseemia is associated with increased mortality and a high APACHE II score ( $P = 0.022$ ). Safavi and Honarmand.<sup>12</sup> also showed increased APACHE II score in hypomagneseemia cases (14.16 vs. 10.80). Limaye *et al.*<sup>13</sup> had found no difference in APACHE II score (14.52 vs. 15.75) in ICU patients between hypomagneseemic and normomagneseemic group. Safavi and Honarmand.<sup>12</sup> showed that ICU stay (9.16 vs. 5.71 days) and total hospital stay (15.29 vs. 12.81 days) are higher in hypomagneseemia group. Limaye *et al.*<sup>13</sup> did not find statistically significant difference. Safavi and Honarmand.<sup>12</sup> and Limaye *et al.*<sup>13</sup> also showed statistically significant difference in need of ventilator support ( $P < 0.05$ ). Hypomagneseemia was associated with increased ventilator requirement ( $P < 0.009$ ) in the current study. The present study shows that hypomagneseemia is associated with increased incidence of hypocalcemia. ( $P = 0.031$ ). Safavi and Honarmand.<sup>12</sup> and Limaye *et al.*<sup>13</sup> also showed similar association. The present study does not show any association with potassium abnormalities the reason for which is difficult to explain. Limaye *et al.*<sup>13</sup> also did not find any association whereas Safavi and Honarmand.<sup>12</sup> showed greater incidence of hypokalemia ( $P < 0.05$ ). There was an increased incidence of sepsis in patients with hypomagneseemia in the present study. ( $P = -0.015$ ) Safavi and Honarmand.<sup>12</sup> and Limaye *et al.*<sup>13</sup> also showed increased incidence of septicemia in hypomagneseemia patients. The present study shows association of hypomagneseemia in critically ill patients with diabetes and hypertension which

concur with Safavi and Honarmand.<sup>12</sup> and Limaye *et al.*<sup>13</sup> Even though the literature shows increased incidence of hypomagneseemia in alcoholics, it is not statistically significant in the present study. There is an increasing trend of alcoholics having hypomagneseemia, even though it is not statistically significant. ( $P = 0.08$ ). Limaye *et al.*<sup>13</sup> also did not find any association.

There are no clear-cut guidelines for the correction of hypomagneseemia. According to Kevin J. Martin *et al.*<sup>14</sup> in cases of severe ( $<1$  mEq/L in the serum) and symptomatic hypomagneseemia, correction is recommended. In asymptomatic patients with relatively mild reductions in serum  $Mg^{++}$  (between 1.0 and 1.5 mEq/L, the significance of hypomagneseemia and hence the need of treatment is not clear.

This study does not show any relation with arrhythmia, neurological manifestations, duration of stay, potassium

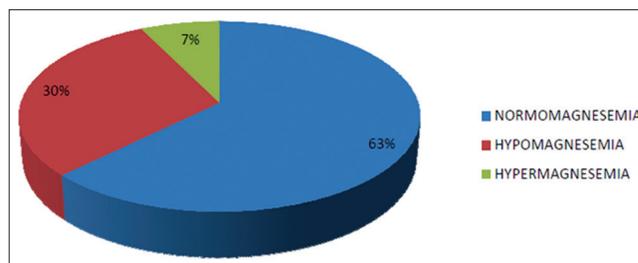


Figure 1: Magnitude of magnesium disturbances

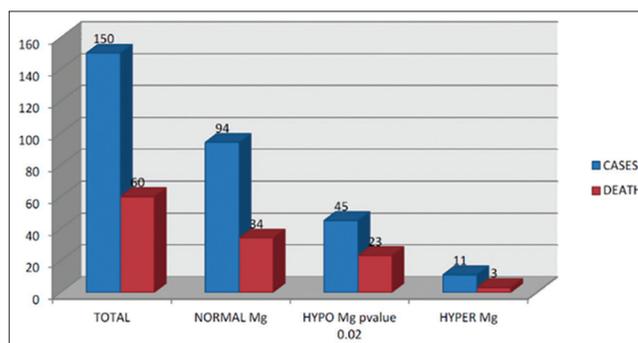


Figure 2: Magnesium and mortality

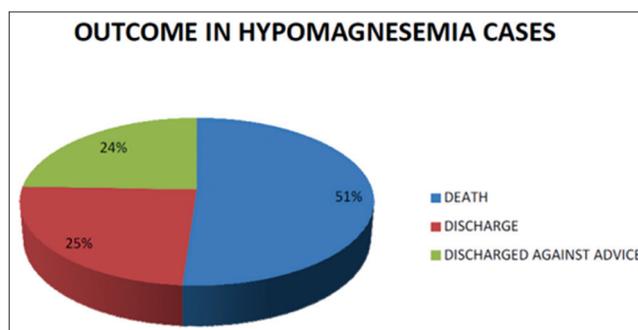


Figure 3: Outcome in hypomagneseemia

disturbances, other electrolyte abnormalities, creatinine levels, metabolic acidosis, inotropic use, type of diet, and anemia. Whether hypomagnesemia in critically ill is a significant abnormality in itself contributing to the causality of complications, which needs to be corrected or is it just an insignificant association without any implications is difficult to ascertain.

### Limitations of this Study

- Total serum magnesium instead of ionized magnesium is measured
- Magnesium levels within first 24 h of admission were only done. Follow-up magnesium levels were not done
- Lack of clear-cut guidelines for treatment of magnesium abnormalities
- This is a descriptive non-interventional study. A large multicentric, randomized, double-blind, interventional, trial for magnesium supplementation in critically ill patients with hypomagnesemia is required in future to evolve a consensus/guidelines for treatment of hypomagnesemia in critically ill.

### CONCLUSION

This study highlights the magnitude of magnesium disturbances on admission in critically ill patients admitted to ICUs under Department of General Medicine of JSS Hospital, Mysore. Hypomagnesemia is associated with high APACHE II score and high mortality. Patients with hypomagnesemia who died had a higher APACHE II score which shows that hypomagnesemia is associated with increased mortality. Patients with hypomagnesemia required ventilator support more frequently. Hypomagnesemia had statistically significant association with the following hypocalcemia, hypoalbuminemia, septicemia, diabetes, and hypertension. This study does not show any relation with arrhythmia, neurological manifestations, duration of stay, potassium

disturbances, other electrolyte abnormalities, creatinine levels, metabolic acidosis, inotropic use, type of diet, and anemia. Whether hypomagnesemia in critically ill is a significant abnormality in itself contributing to the causality of complications, which needs to be corrected or is it just an insignificant association without any implications is difficult to ascertain.

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# Efficacy and Safety of Cervical Epidural Anesthesia for Thyroid Surgery

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## Abstract

**Background:** Cervical epidural anesthesia (CEA) has been employed successfully for various types of surgical procedures involving upper limb surgery, thoracic wall surgery, carotid artery surgery, and neck dissections. Anesthesia for thyroidectomy in a patient with tracheal deviation due to the large size or altered functional status of the thyroid can be complicated. Endotracheal intubation is difficult in such cases and more prone to cardiac arrhythmia under the influence of inhalational anesthetics.

**Objectives:** This prospective study was designed to assess the effectiveness and safety of CEA for thyroid surgery.

**Materials and Methods:** Patients were divided on an alternate basis into two groups of 25 each. Group A to receive 10 ml of local anesthetic (1% lignocaine with adrenaline). Group B to receive conventional general anesthesia (GA) with endotracheal tube intubation. We compared their efficacy in terms of hemodynamic parameters, pulmonary parameters, blockade quality, and complications.

**Results:** Of the total study: In Group A, 25 patients completed the study successfully. Sensory block attained the median dermatomal range of C<sub>2</sub>-T<sub>4/5</sub>. Hemodynamic parameters and respiratory parameters decreased, but none of the patients had any complications. In Group B, 25 patients received GA. Hemodynamic parameters and respiratory parameters in the beginning and end of the procedure were increased, attributed to intubation and extubation. Post-operative pain that required rescues analgesics.

**Conclusion:** Cervical epidural route can be considered as a safe alternative to conventional GA for patients undergoing thyroid surgery where difficult intubation is anticipated and vulnerable to cardiovascular complications.

**Key words:** Anesthesia, Cervical epidural, General anesthesia, Neck dissection

## INTRODUCTION

Thyroid surgeries are conventionally performed under general anesthesia (GA).<sup>1</sup> Safe and effective anesthesia for thyroid surgery can become a problem for the anesthesiologists; this becomes especially relevant in large goiter with tracheal deviation.<sup>2</sup> Endotracheal intubation is difficult in such cases, and can be hazardous if associated

with functional thyroid disorders.<sup>3</sup> Patients with hypo and hyperthyroidism are more prone to cardiac rhythm disorders that might get aggravated under the influence of GA agents.<sup>4,5</sup>

Regional anesthetic techniques are safer than GA in high-risk patients where endotracheal intubation is difficult or cardiac arrhythmias are anticipated.<sup>6</sup> Regional anesthesia is not a conventional option for thyroid surgery. Cervical epidural anesthesia (CEA) has been employed successfully for various types of surgical procedures involving thoracic wall surgery,<sup>7,8</sup> carotid artery surgery,<sup>9,10</sup> upper limb surgery,<sup>11-13</sup> and neck dissections<sup>12</sup> with good results, so CEA provides an alternate choice for thyroid surgery. Here, we describe our experiences of using this technique for thyroid surgery.<sup>14,15</sup>

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## MATERIALS AND METHODS

Total 50 patients of ASA physical Status I-II, aged 18-60 years, posted for thyroid surgery, over a period of 2-year, were included in the prospective study conducted in Bidar Institute of Medical Sciences, Bidar. Ethical clearance was obtained by Ethical Committee Approval and written informed consent was also obtained from subjects. Patients were randomly divided into one of the two groups (25 each).

Pre-anesthetic check-up was done. A detailed case history was taken along with general physical examination and systemic examination. Airway assessment and spinal column examination were done. The following laboratory examination were done in selected cases - Hemoglobin, urine analysis, blood sugar, blood urea, serum creatinine, coagulation profile, blood grouping and Rh typing, electrocardiogram (ECG), chest X-ray, fine needle aspiration cytology, and ultrasound neck. X-ray neck anteroposterior and lateral view were taken when suspected tracheal deviation was present. Bedside pulmonary function tests were also done. The size of the thyroid, medical comorbidities, and difficult intubation evaluated before the surgery. The procedure of CEA explained, and the patient was informed to communicate to the anesthesiologist about the perception of any pain or discomfort during the surgery.

Cases randomly allotted to either group of elective thyroidectomy alternatively under CEA and GA as per the preplanned protocol.

- Group A to receive 10 ml of local anesthetic (1% lignocaine with adrenaline)
- Group B to receive conventional GA with endotracheal tube intubation.

We compared their efficacy in terms of hemodynamic parameters, pulmonary parameters, blockade quality, and complications.

### The Technique of CEA

On arrival to the operation theater, standard monitors were attached; an intravenous access was achieved with 18 gauge cannula and patient positioned in the lateral decubitus position with the neck flexed and chins on the chest. Under strict aseptic precautions the neck was prepared and draped, cervical epidural space was identified with an 18 gauge Tuohy epidural needle, at the C<sub>7</sub>-T<sub>1</sub> interspaces using the loss of resistance technique. An epidural catheter was then introduced 4 cm into the epidural space. After negative aspiration, the catheter was secured in place, and patients were made to lie supine. The test dose, 1% lignocaine with adrenaline (3 ml) was injected via an epidural catheter; vitals

(ECG, heart rate [HR], noninvasive blood pressure (BP), SpO<sub>2</sub>, respiratory rate, and consciousness), were monitored for 5-10 min for any sign of a complication. In the absence of such signs 7-10 ml of lignocaine with adrenaline was further injected through the epidural catheter. The sensory blockade assessed by response to pinprick method in an ascending fashion starting from the T<sub>12</sub> dermatome (the onset of sensory block was defined as the time to loss of sensation to pinprick in the C<sub>3</sub> dermatome). Hemodynamic parameters monitored before and after the blockade.

The patients were maintained in a state of conscious sedation with midazolam (mean dose, 0.05 mg/kg IV) throughout the surgery. Vocal cord functions were monitored intermittently by verbal communication with the patient. Any intraoperative discomfort in the neck or request for pain relief was managed by administering epidural top-up of 5-8 ml of 1% lignocaine with adrenaline. Post-operative, monitoring of vital signs, visual analogue scale (VAS) scores and sedation scores were done. The incidence of hypotension (arterial BP <20% of baseline), bradycardia (HR <50 beats/min), nausea, vomiting monitored in the recovery room. Epidural top-ups were given on complaints of pain by the patient using 5 ml of 0.125% of bupivacaine.

Sedation scores were assessed every 15 min both intraoperative and post-operative using a four-point score described by Chernin *et al.*

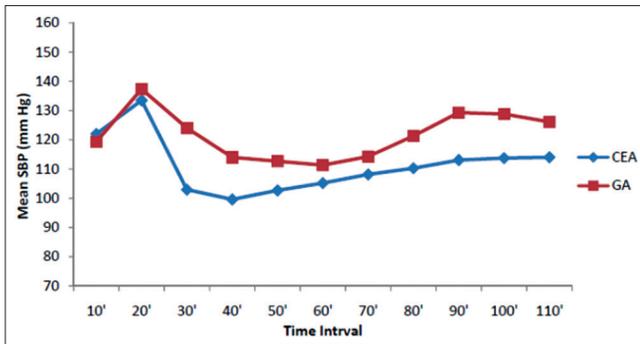
- Grade 0: Patient wide awake
- Grade 1: Patient is sleeping comfortably, but responding to verbal commands
- Grade 2: Deep sleep but arousable
- Grade 3: Deep sleep, unarousable.

### GA

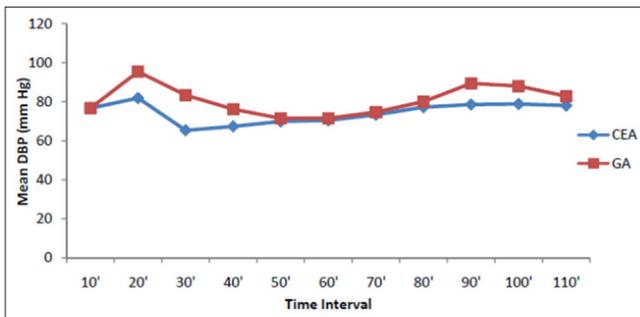
After usual premedication with intravenous glycopyrrolate, midazolam and fentanyl, induction was done using intravenous thiopentone sodium followed by intravenous succinylcholine. The airway was secured using appropriate size endotracheal tube and fixed after confirming bilateral air entry equal. The patient was maintained on oxygen, nitrous oxide, isoflurane and intravenous vecuronium. Ketamine and halothane were avoided. The patient was reversed with neostigmine and glycopyrrolate and extubation done after airway reflexes intact.

Throughout the perioperative period, pulse rate, BP, respiratory rate, ECG, and SpO<sub>2</sub> were monitored in all the patients.

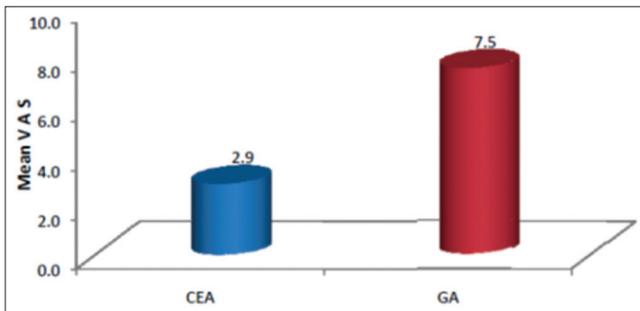
The Statistical software namely SPSS 19.0, Stata 8.0, were used for the analysis of the data and Microsoft Word and Excel have been used to generate Graphs 1-3, Table 1, etc.



Graph 1: Changes in systolic blood pressure



Graph 2: Changes in diastolic blood pressure



Graph 3: Distribution of VAS scale

Table 1: Age distribution

Age	Sex		Total
	Female	Male	
15-25	5	1	7
26-35	10	7	20
36-45	16	3	21
46-55	8	2	10
>55	1	1	2
Total	36	14	50

**RESULTS**

The study consisted of 50 patients for ASA physical Status I-II, aged 18-60 years, posted for thyroid surgery. The technique of CEA was successful in 25 out of 28 patients in whom it was attempted (one patient had patchy block, and two patients had hemorrhagic

tap). The median time of duration of surgery was 70 min (50-90 min). No patient reported pain during the procedure. The upper margin of sensory block was assessed in C<sub>2/3</sub> dermatome in all patients, and the median of the lower margin of sensory block was T<sub>4/5</sub> (minimal extent C<sub>2</sub>-T<sub>1</sub>; maximal extent C<sub>2</sub>-T<sub>10</sub>). The patients were not in distress during surgery and did not complain of dyspnea during the procedure and in the post-operative period. There was no case of dura mater puncture. Patients were comfortably maintained sedated but awake during the procedure with no untoward effect. Monitoring of the vitals was carried out, and all patients' vital parameters were within normal limits, none of the patient's required additional intervention.

GA performed in 25 patients following normal induction and intubation, except for one case that had difficulty in intubation due to large goiter and deviated trachea.

**Age Distribution**

50% of the patients in the study were in the age group between 16 and 45 years.

**Systolic BP**

Before surgery, systolic BP was found to be normal in both the groups. Intraoperative, Mean systolic BP in the CEA group to be 108.36 ± 5.4 mm of Hg and GA group was 126.24 ± 10.5 mm of Hg. In both the groups, the systolic BP remained within normal limits. In the GA group, there was an increase in systolic BP and was attributed to intubation and extubation. Statistically, there were no significant changes in both the two groups (P > 0.05).

**Diastolic BP**

Diastolic BP was found to be normal in both the groups preoperatively. The Mean Diastolic BP in the CEA group to be 70.3 ± 6.3 mm of Hg and GA group was 76.2 ± 12.14 mm of Hg. In the GA group, there was an increase diastolic in BP and was attributed to intubation and extubation. Statistically, there were no significant changes in both the two groups (P > 0.05).

**HR**

The mean pulse rate in the CEA group to be 68.5 ± 5.4/min and GA group was 80.29 ± 8.48 per min. The pulse rate remained normal in both the groups; however, CEA group had lower readings compared to GA. There was no need of any additional intervention required. Statistically, there were no significant changes in both the two groups (P > 0.05).

**SpO<sub>2</sub>**

There were no significant changes in oxygen saturation in both the groups. The mean SpO<sub>2</sub> in the CEA group to be 98.02 ± 1.06 and GA group was 98.95 ± 0.6. Statistically,

there were no significant changes in both the two groups ( $P > 0.05$ ).

### Respiratory Rate

The mean respiratory rate in the CEA group found to be increased ( $25 \pm 3/\text{min}$ ). In GA group controlled ventilation was done ( $16 \pm 2/\text{min}$ ).

### Post-operative

#### Pulmonary function tests

Forced expiratory volume (FEV) and forced vital capacity (FVC) decreased by 10-15%, but these changes were not clinically significant. Statistically, there were no significant changes in the pulmonary parameters between the two groups ( $P > 0.05$ ).

#### Pain

Post-operative pain is comparatively less in the cervical epidural group with VAS of 3 as compared to GA group with the VAS of 7.5. Statistically, there were significant changes in the Post-operative pain between the two groups at corresponding time intervals with significance value  $< 0.05$ .

## DISCUSSION

The efficacy of CEA compared with GA in terms of hemodynamic changes, pulmonary changes, quality of blockade and complications.

### Hemodynamic changes

In CEA blockade of sympathetic fibers consequently decreases HR, cardiac output and contractility. The mean BP is unchanged/decreased depending on peripheral systemic vascular resistance. The baroreflex activity is also partly impaired. CEA can be beneficial to the patients with limited cardiac reserve due to prolongation of coronary perfusion time and decreased ventricular after load. In our study, the HR is slightly lower in CEA compared with GA and clinically not significant. BP remains within normal limits, toward the beginning and end of procedure there was an increase in BP in GA group was attributed to intubation and extubation.

Jain<sup>3</sup> HR decreased significantly in all the three groups. No vasopressor agent was required in any of the cases; however, two patients developed one episode of bradycardia, which was managed promptly by a bolus dose of atropine 0.6 mg IV.

Macchiarini *et al.*,<sup>5</sup>: CEA results in the sympathetic blockade and thereby reduces the HR, cardiac output and myocardial contractility. BP decreases or remains unchanged depending on the systemic vascular changes. Sympathetic blockade also reduces myocardial ischemia

Capdevila *et al.*,<sup>16</sup>: The major concern with CEA has been its effects on HR and hemodynamic stability. CEA blocks the sympathetic cardiac accelerator fibers that arise at T<sub>1</sub>-T<sub>4</sub>. Consequently decreases HR, cardiac output and contractility. The most frequently reported side effects of CEA are hypotension in 10.9% and bradycardia in 2.8%.

### Pulmonary parameters

Effects of CEA on respiratory function especially phrenic nerve controlled diaphragmatic movements. Lignocaine with adrenaline when used in a lower concentration of 1%, in the epidural space, the diaphragmatic function is not affected. Hence, we used 1% lignocaine for this study. Pulmonary function test after CEA decreased by 10-15%, were clinically not significant comparative to GA.<sup>17-19</sup>

Jain<sup>3</sup> Pulmonary variables demonstrated a significant decline in FVC and FEV1 in all the patients, none of the patients developed dyspnea or hoarseness during the perioperative period.

Stevens *et al.*,<sup>15</sup> found a measurable reduction in bedside pulmonary function test after CEA. They found that the FEV and FVC decreased by 12-16% after using 300 mg of lignocaine, but these changes were not clinically significant. They concluded that the motor block of phrenic nerve was incomplete after CEA.

Santpur *et al.*,<sup>5</sup> CEA causes minimal respiratory and hemodynamic inhibition and hence the technique was preferred in chronic obstructive pulmonary disease patients. Groeben *et al.* found no significant changes in lung functions under high thoracic segmental epidural anesthesia with ropivacaine or bupivacaine in patients with severe obstructive pulmonary disease undergoing breast surgeries.

Shilpashri<sup>1</sup> CEA decreases for post-operative pain in high-risk patients can improve pulmonary functions by reducing the incidence of pneumonia and respiratory failure, improving oxygenation, decreasing the duration of mechanical ventilator support while hemodynamic parameters remain normal. In our study, the hemodynamic and respiratory changes were similar to finding concluded by Shilpashri *et al.*

### Blockade quality

The segment of sensory block seen in CEA was from C<sub>2</sub>-T<sub>4/5</sub> dermatome in all the patients. Median time to onset of the sensory block is 10 min. Most studies have successfully conducted surgeries under CEA using 10-15 ml of local anesthetic volumes. The local anesthetic required is approximately 1.0 and 1.5 ml a segment in cervical and thoracic epidural space, respectively (i.e., nearly 10-15 ml volume for spread to 8 to 10 segments).<sup>4</sup> In our study, we have used 10 ml of 1% lignocaine with adrenaline initially

and top up a dose of 5 ml was given when required, all patients had an excellent blockade.

### Complications

Thyroidectomy under GA, in patients with goiter is associated with:

- Difficult and traumatic intubation in cases of tracheal deviation and compression
- Arrhythmias with the use of anesthetic gases like halothane
- Intubation stress response in associated co-morbid conditions
- Polypharmacy
- Post-operative nausea and vomiting
- Post-operative pain requires more rescue analgesia.

CEA is found to be a suitable alternative to GA in all the problems above. CEA is not practiced in routine anesthesia, commonly due to operator inexperience and risk of potential complications such as a dural puncture, neurovascular injury, epidural bleed/hematoma, or abscess formation. Bonnet *et al.* noted, dural puncture in 2 (0.5%) and epidural venipuncture in 6 (1.5%) patients, in a retrospective analysis of 394 patients. Hakl *et al.* reported bloody epidural tap in four patients, migration of local anesthetic solution into subarachnoid space in six patients and failed epidural puncture in three patients. We observed a hemorrhagic tap in two patients during epidural space localization thus mandating conversion to GA. None of our patients had a dural puncture. Previous studies have documented a proportionately higher risk of hypotension and arrhythmias during thyroid surgeries under GA.<sup>20-22</sup>

In contrast, Khanna and Singh mentioned no cardiovascular complications during thyroid surgeries under CEA.<sup>2</sup>

CEA has gained popularity due to its safety, stable hemodynamic and pulmonary parameters. Furthermore, decreases the stress response by excellent pain relief and enhances early post-operative recovery with minimal morbidity<sup>2,14</sup> we used CEA as sole anesthetic technique for thyroid surgery.

It has several advantages. Patients are operated under CEA can be maintained in a state of conscious-sedation. The relative bloodless field and the possibility of monitoring the vocal cord movements using the verbal contact in a conscious patient during surgery is a distinct advantage of this procedure. Other noted benefits of epidural anesthesia are (1) less bleeding, (2) lack of electrolyte imbalance, (3) early ambulation and recovery, (4) no post-operative atelectasis of lung, (5) minimum BP drop, (6) little nausea or vomiting, (7) no vascular spasms or post-operative

phlebothrombosis, and (8) little or no motor nerve block.

In our study, respiratory and hemodynamic functions were within normal limits and other complications were not observed, thereby proving that epidural anesthesia can be immensely useful as a sole anesthetic agent for thyroid surgeries.

## CONCLUSION

CEA provides stable vital parameters, excellent control of pain extending into post-operative period and early recovery with reduction in stress response, blood loss and post-operative morbidity; we conclude that CEA can be used as a safe alternative to GA for thyroid surgeries, especially in patients with co-morbidities of respiratory system, cardiovascular system and deranged thyroid profiles.

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# A Simple New Method to Retrieve the Impacted Balloon Catheter: A Clinical Study

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## Abstract

**Introduction:** A urinary catheter is any tube system placed in the body to drain and collect urine from the bladder. Urinary catheters are sometimes recommended as a way to manage urinary incontinence and urinary retention in both men and women. There are different types of catheters, which may be used for a variety of different reasons, either for Use of a catheter for short-term use or long-term use. Long-term use catheters are called indwelling catheters. We are using past 24 years with the devised technique for retrieving the impacted balloon catheter either per urethral or suprapubic. It is simple, easy, and does not require any equipment or operation theater. It is bedside procedure.

**Purpose:** The retained and impacted Foley's catheter, which are failed to remove by other methods can be removed with a simpler technique.

**Methods:** Various methods are available to remove retained Foley's catheters. We have done a randomized prospective study of retained Foley's catheters removal. We simply insert ureteric catheter stylette or wire which is introduced into the channel of balloon inflation. By this water leaks out and catheter comes out. We have done hundreds of cases past 24 years in a government hospital in bedside as well in the outpatient department. No complication or failure occurred.

**Results:** The results are excellent with this technique for removal retained Foley's catheters, and it is simple to do the procedure.

**Conclusion:** This method is simple, safe, inexpensive, and can be carried out without anesthesia ultrasound facilities and radiological facilities are not available. We are using this method over past 24 years with 100% success and without any complications.

**Key words:** Foley's catheter, Impacted balloon, Retrieving impacted catheter and suprapubic catheters

## INTRODUCTION

Catheters come in a large variety of sizes, materials (latex, silicone, Teflon), and types (Foley catheter, straight catheter, and coude tip catheter). For example, a Foley catheter is a soft plastic or rubber tube that is inserted into the bladder to drain the urine.<sup>1-3</sup>

Foley's catheter is the most commonly used a self-retaining catheter. The problem of impaction of the Foley catheter

(local made) is commonly encountered in day to day clinical practice. Most of the times cases are referred to the outpatient department or bedside calls for this problem. Most of the times catheter is cut short just distal to the external meatus.<sup>4,5</sup>

Various conventional methods available at the present results in failure of 40% cases. The techniques available are:

1. Ether technique - Banned due to ether chemical pyelitis
2. Over filling and rupture of balloon - Banned due to residual balloon pieces in bladder and rarely rupture bladder
3. Suprapubic puncture of balloon blindly or ultrasound guided
4. Per rectal palpation of balloon and puncturing with needle

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5. Catheter telescoping for retrieval of impacted catheter
6. Suprapubic cystostomy as the last resort to retrieve the catheter.

We have devised a technique using past 24 years, tried on hundreds of patients for impacted balloon catheters. It doesn't require any extra equipment.

## METHODS

The patient is kept in supine position. After aseptic precaution, the procedure is followed to remove retained Foley's catheter.

### Technique

The Foleys catheter made up of latex material. To inflate the balloon water is injected into the luer lock of a side channel of the catheter. The catheter gets stuck when the latex particle acts like ball valve system and does not allow water to be withdrawn Figure 1.

We simply insert ureteric catheter stylette or wire which is introduced into the channel of balloon inflation (Foley's catheter is already cut). Slowly, water of balloon drains out beside the stylette. Within few minutes, catheter gets deflated and can be removed Figures 2 and 3.

## RESULTS

Experts recommend that the smallest possible catheter is used. Some people may require larger catheters to control leakage of urine around the catheter, or if the urine is thick and bloody or contains large amounts of sediment.

### Catheter placement details

Retained suprapubic catheters	10% cases
Retained per urethral catheters	90% cases

We have done hundreds of cases without any failure with this technique. We have not included the calcified catheters stuck in this study.

### Male and female ratio

Males	87% cases
Females	13% cases

### Age of occurrence of retained Foley's catheter

0-10	3% cases
10-20	16% cases
20-30	19% cases
30-40	13% cases
40-50	15% cases
50-60	27% cases
Above 60 years	7% cases



Figure 1: Stuck Foley's catheter *in situ*



Figure 2: Stylette *in situ* with water being drained

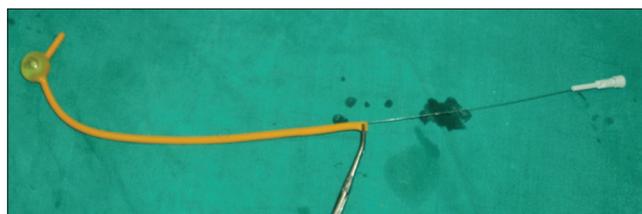


Figure 3: *Demo vitro* photo

## DISCUSSION

Using ether by injecting into the balloon channel will blasting the balloon and sometimes pieces of the catheter are left behind, and they act as a nidus for calculus formation. By puncturing the bulb under ultrasound guidance suprapubically is painful. A rectally using gloved finger guidance in the lithotomy position with needle puncture of the balloon is inconvenient. Failing various methods people have rarely had done through open suprapubic surgery.

The technique used by us is simple and does not require any expertise and reproducible results. In this aspect, our technique is very superior.

We should be aware that larger catheters are more likely to cause damage to the urethra. Using large catheters can cause urethra ulcerations, sinus formation, and urethra fistula formation; some people have developed allergies or sensitivity to latex after long-term latex catheter use. These people should use the silicone or Teflon catheters. Long-term urethral Catheters means a catheter that is left in place for a period of time may be attached to a drainage bag to collect the urine.<sup>5-7</sup>

Most experts advise against routine changing (replacing) of the catheters once in 3-4 weeks. If the catheter is clogged, painful, or infected it may require immediate replacement.<sup>8,9</sup>

There are potential complications like fever, chills, foul smelling urine, balanitis, bleeding into or around the catheter; catheter is not draining or leakage of large amounts of urine can occur during prolonged catheterisation.<sup>10,11</sup>

## CONCLUSION

We are using this method over past 24 years with 100% success and without any complications. Using ureteric catheter stylette or wire for deflating balloon does not

require in this special expertise. This technique is simple to follow and to learn.

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# Clinical Profile of Atypical Manifestations of Diseases in Elderly Patients Admitted to Critical Care Areas

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## Abstract

**Background:** As the life expectancy goes up, it brings new challenges and dimensions, especially in a developing country like ours. In India, the geriatric age group above 60 years is expected to double from 7.7% in 2001 to 12.30% in 2025. Diseases may present in an atypical manner in elderly.

**Materials and Methods:** This is a prospective, longitudinal, observational, descriptive study. "Geriatric patients" defined as aged 60 years and older, from both sexes were enrolled for this study over a period of 2-years.

**Results:** Of the 10,560 patients admitted under general internal medicine during the study period, 32.76% of cases, i.e., 3450 patients qualified to be called as "geriatric patients," of whom 710 patients, i.e., 20.58% of the geriatric admissions were in critical care areas. Nearly 55%, of the patients, stayed in the intensive care unit (ICU) setting inclusive of ICU, respiratory ICU and intensive coronary care unit (ICCU) during the study period of whom 61.8% of the subjects presented with typical symptoms and the rest presented with atypical symptoms. A higher death rate among elderly presenting with atypical manifestations was observed. 30.42% of the patients were admitted to ICCU with nearly two-thirds presenting typically and one-third atypically and stayed for a mean duration of 3.17 and 3.54 days, respectively.

**Conclusion:** Clinical presentations and outcome of diseases may be different in geriatric age group as a result of which the diagnosis and management process of critical illnesses in the elderly population may become difficult and complicated. An awareness of atypical manifestations and hence high index of suspicion is a must while managing elderly patients.

**Key words:** Atypical presentations, Elderly, Geriatric

## INTRODUCTION

Aging is a nature ordained, inevitable phenomenon. As the life expectancy goes up, it brings in new challenges and dimensions, especially in a developing country like ours. In India, the geriatric age group above 60 years is expected to double from 7.7% in 2001 to 12.30% in 2025.<sup>1</sup> Definitions of the old, elderly, aged and aging are confusing. They

could mean different in different nations and cultures. The definitions may be different for both sexes as aging may be affected by different situations during the lifetime.<sup>2</sup> A chronological definition has been attempted but has become fodder for debates. UN figures for both 60 and 65 years of age and above are available.<sup>3</sup> In view of the socio-economic milieu in India, age 60, as the threshold appears to be a more reasonable and realistic one when compared to age 65 elsewhere.<sup>4</sup> As elderly patients are a group at risk of various ailments, they are also the most common group to utilize hospital services, including critical care.

Diseases may present in atypical manner in both extremes of age. The presentations of acute myocardial infarction (AMI) could be atypical in the elderly.<sup>5</sup> The typical crushing

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retrosternal pain could be a common presentation even in the elderly; yet we come across atypical presentations (such as acute confusion, syncope, atypical chest pain, congestive heart failure, vomiting, or weakness) in clinical practice as well as just fatigue or shortness of breath alone which could be the only manifestation. Atypical presentations of infections such as lower respiratory tract infection-pneumonia and urinary tract infections (UTI), such as confusion and altered sensorium, are also encountered in clinical practice. Misdiagnosis and missed diagnosis in this age group because of atypical manifestations is a cause of concern.<sup>5</sup>

Data on critical care medical geriatrics is scanty. The current study could serve as a guide for effective planning of geriatric health care services. Over a period of 2-years, we conducted a study of patients admitted to “critical care areas (CCAs)” (consisting of the medical intensive care unit, respiratory ICU [RICU], intensive coronary care unit [ICCU], and emergency wards [EW]) under the Department of General Medicine of a teaching tertiary care referral hospital at Mysore, Karnataka state, South India. We set out with an objective of compiling a clinical profile of geriatric in-patients hospitalized in CCAs of Medicine with special reference to atypical manifestations of various critical illnesses in the elderly.

## MATERIALS AND METHODS

Institutional Ethics Committee Approval was obtained. This is a prospective, longitudinal, observational, descriptive study. “Geriatric patients” defined as aged 60 years and older,<sup>4</sup> from both sexes were enrolled for this study over a period of 2-years. All persons of >60 completed years of age, of both sexes admitted in CCAs of JSS Hospital under Internal Medicine during the study period were included. Written Informed consent was obtained in all cases. Elderly patients presenting with surgical emergencies and trauma, and patients admitted directly to non-CCAs/low dependency units, i.e., general and special wards were excluded from the study. The hospitalization details were collected from the in-hospital records. Data were entered in Microsoft Excel, and statistical calculations were done through SPSS 16.0 (2007) for windows. The statistical method used was descriptive statistics. A total of 10,560 patients were admitted under the department of general internal medicine during the study period out of whom 32.76% of cases, i.e., 3450 patients were above 60 years of age, of whom 710 patients, i.e., 20.58% of the geriatric admissions were admitted in CCAs of the department consisting of the ICU, RICU, ICCU, and EW, under all the medical units.

## RESULTS

Of the 10,560 patients admitted under general internal medicine during the study period, 32.76% of cases, i.e., 3450 patients qualified to be called as “geriatric patients,” of whom 710 patients, i.e., 20.58% of the geriatric admissions were in CCAs (Figure 1). The majority (61.26%) of the study subjects were rural patients. Males predominated over the females as study subjects in a ratio of 1.6:1, i.e., 437 males:273 females. Maximum admissions were in 60-65 age groups with a gradual decline thereafter. Discharge rate was 57.74%, discharge against medical advice was 23.8% (Figure 2). In-hospital death was seen in 15.5%.

270 patients were current smokers, 176 consumed alcohol, 30 were tobacco quid chewers. The more the number of disease entities (diagnoses) per patient, the more was the likelihood of being in CCA. Mean duration of hospitalization of the study population was 8.3 days for

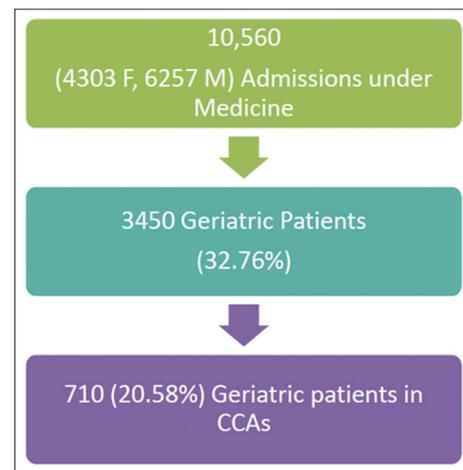


Figure 1: Method of collection of cases

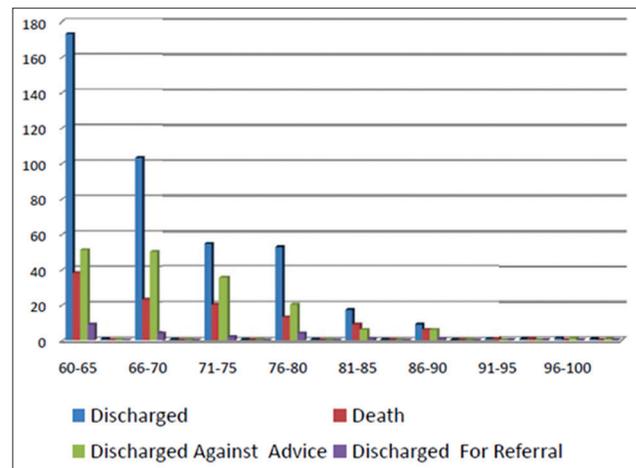


Figure 2: Age group and outcome

cases presenting with both typical and atypical symptoms. Mean duration of critical care stay inclusive of EW, ICU, ICCU, and RICU was 4.56 days for typical presentation and 4.94 days for those with atypical presentation. Nearly, 55% of the patients, stayed in the ICU setting inclusive of ICU, RICU, and ICCU during the study period of whom 61.8% of the subjects presented with typical symptoms and the rest presented with atypical symptoms. 30.42% of the patients were admitted to ICCU with nearly two-thirds presenting typically and one-third atypically and stayed for a mean duration of 3.17 and 3.54 days, respectively. The majority of the patients in the CCAs stayed in the EW, i.e., 64.5% with nearly two-thirds presenting typically and one-thirds presenting atypically and duration of stay in the EW for 3.75 days for typical and 4.12 days for atypical cases. 65.5% of the patients admitted to ICUs were put on mechanical ventilator for a time duration of 1-13 days with a mean of 3.7, standard deviation 2.3 days, 50% were hypertensives, 38.8% were diabetics, 23.23% had both hypertension (HTN) and diabetes mellitus (DM), and 16.05% had ischemic heart disease (IHD). 4.64% of the total study population had HTN, DM, and IHD. 14.5% had chronic obstructive pulmonary disease. HIV infection (newly detected on present admission) was seen in 3 individuals, a prevalence of 0.4%, which was a significant finding. Metabolic encephalopathy was seen in 12.4% of all the geriatric individuals admitted in the critical care setting. The most common cause of metabolic encephalopathy was hypoglycemic encephalopathy, followed by hyponatremic encephalopathy, sepsis-related encephalopathy, and hepatic encephalopathy in that order. The cause of encephalopathy could not be established in 15 individuals.

34.5% presented with atypical manifestations. Atypical manifestations were significant in those with acute coronary syndromes (ACS), UTI and pneumonia and not so in CVA and heart failure. Manifestations of disease can be significantly atypical in elderly, most commonly in ACS and Infections. Overall, among the elderly geriatric population, 34.5% presented with atypical manifestations not typical of the primary reason for critical care admission and this observation was statistically significant. Another observation made was a higher death rate among elderly presenting with atypical manifestations (Figure 3). A total of 98 patients out of 710, i.e., 13.8% of the study population had acute coronary syndromes. Most common among the ACS was ST-elevation myocardial infarction (STEMI), followed by non-STEMI (NSTEMI). A higher proportion of patients presented with atypical symptoms as compared to those who presented with typical symptoms of ACS in both the STEMI and

NSTEMI groups and this observation was statistically highly significant (Figure 4). In the diagnosis of ACS, of the atypical complaints with which the patients presented, breathlessness was the most common complaint followed by atypical chest pain including right sided chest pain and a burning sensation in the chest. Generalized weakness and fatigue was the third most common atypical presenting complaint. Vague chest discomfort different from chest pain was seen as the fourth common atypical symptom. Upper abdominal/epigastric pain was also complained by a few patients.

Respiratory infections in the elderly in CCAs were seen in 173 out of the 710, i.e., 37% of whom 51.5% presented with typical presentation and the rest 48.5% presented atypically. 23.1% of the patients had bronchopneumonia of which 52.5% presented typically and 47.5% presented atypically. 25.4% of the patients had aspiration pneumonia of whom 56.8% presented typically and 43.2% presented atypically. Of the atypical presenting complaints, breathlessness, and

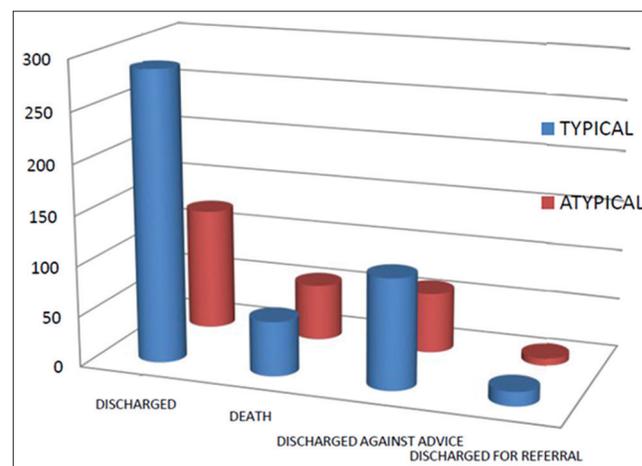


Figure 3: Outcome in typical and atypical presentation

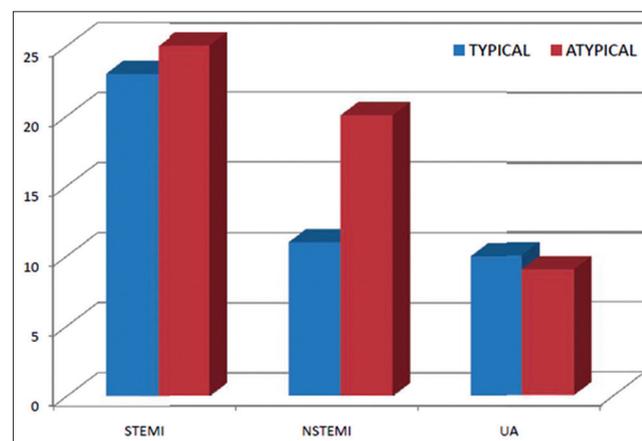


Figure 4: Presentations of acute coronary syndromes

disorientation were the more common atypical symptoms of respiratory infection.

Urinary tract infection was observed in 6.3% of the study population of whom 10.2% presented with atypical symptoms as opposed to 4.3%, i.e., those presenting with typical symptoms and this difference was statistically significant. In UTI inclusive of cystitis, urethritis, pyelonephritis and perinephric abscess, prostatitis, altered sensorium was the most common atypical symptom followed by generalized weakness and fatigue.

## DISCUSSION

In this study, overall, among the elderly geriatric patients admitted to CCAs, 34.5% presented with atypical manifestations not typical of the primary reason for critical care admission and this observation was statistically significant. Another observation made was a higher death rate among elderly presenting with atypical manifestations.

Clinical implications *vis a vis*. physiological perturbations in the elderly are worth exploring. Elderly patients may have an atypical presentation of different entity, for example, altered mental status due to underlying fluid and electrolyte disorder or infections. It is likely that the final diagnosis reported on paper for an admitted elderly patient may not reflect or explain the basic cause which brought the patient to the hospital in the first place and may not reflect the course in the hospital and eventual outcome or recovery.<sup>6</sup> Bayer *et al.* reported the varied manifestations of AMI in elderly patients.<sup>7</sup> In extreme old age (>85 years), atypical presentations may be dubbed as a rule rather than an exception and the physician must be alert in most acutely ill patients. Furthermore, community-acquired pneumonia in the geriatric age group may present in a different way. The atypical presentation and hence mis/missed diagnosis may result in a dangerous delay of antimicrobial therapy adding to the higher mortality of community-acquired pneumonia in the geriatric age group *vis a vis*. younger patients.<sup>8</sup>

Thus, diseases could be deceptive with atypical presentations in the elderly and the physicians in their day-to-day practice should be on high alert and factor this in.<sup>9</sup> Silent MI in elderly, detected incidentally on electrocardiogram (ECG) is high, ranging between 38% and 60%.<sup>10,11</sup> Moreover, NSTEMI is common in the elderly population, and ECG diagnosis may be difficult to come by. Recognition of the fact that elderly patients with AMI differ in clinical presentation compared to others may guide us in decreasing

both mortality and morbidity in this vulnerable age group. Many authors have elucidated the atypical clinical presentations of AMI in the elderly.<sup>12-14</sup> Dyspnea and other nonspecific symptoms such as giddiness; syncope, and abdominal pain are common in elderly compared to others. Occurrence of nonspecific symptoms in elderly could be because of preoccupation with other non-cardiac problems, or elderly could find it difficult to remember and/or narrate the history correctly and objectively or probably due to a different pain threshold.<sup>15</sup>

### Limitations of the Study are

- The study population included only those presenting to the critical care setting who are not representative of the population at large
- Outcome of those patients who were discharged against medical advice is not known.

Further large-scale multicentric studies of a similar kind will help to throw more light on problems of critical care geriatrics.

## CONCLUSION

Clinical presentations and outcome of diseases may be different in geriatric age group as a result of which the diagnosis and management process of critical illnesses in the elderly population may become difficult and complicated. An awareness of atypical manifestations and hence high index of suspicion is a must while managing elderly patients.

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# Subdural Empyema: Late Complication of Head Injury

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## Abstract

Subdural empyema is a rare intracranial infection. It warrants prompt management to reduce morbidity and avoid mortality. However, clinical and radiologic features may be subtle. Thus, a diagnosis of subdural empyema should not be ignored, especially in a patient with the history of head trauma. We present a case of an adult male with a subdural empyema, who presented with fever, headache and left sided weakness who suffered from head injury 2 years back. He had right frontal sinus fracture with cerebrospinal fluid leak from nose for 3-4 days that subsided. Intracranial complications, subdural empyema can be a delayed complication of head injury that is rare and should be considered.

**Key words:** Abscess, Head injury, Subdural empyema

## INTRODUCTION

Complications of head injury such as subdural empyema are rarely seen, have long-term morbidity if not diagnosed and managed promptly and appropriately.<sup>1,2</sup> The frontal region is the most common location, and it is caused by frontal sinus fracture and chronic frontal sinusitis associated to nasal polyposis. Meningitis and encephalitis are often the first diagnosis considered in this case, space-occupying lesions such as abscesses or subdural empyemas must be considered as well, in particular when there are neurologic deficits, altered mental status or seizures at presentation. We present a case of an adult male who presented with fever, headache, had history of cerebrospinal fluid rhinorrhea and head injury 2 years back, with subdural empyema.

## CASE REPORT

A 32-year-old patient was admitted to the medicine department with complaints of a headache, and fever (on and off) since 3 weeks. 2 years back, he hit his head against a door and had watery discharge coming out of his

nose that stopped after 3-4 days, spontaneously without treatment.

On examination, the patient was conscious and oriented. His vital pulse of 84 beats/min, blood pressure of 120/80 mmHg and temperature of 101° F. Patient had no signs of meningitis, sinus tenderness, ear or nasal discharge. His neurologic examination revealed no abnormality except left hemiparesis. His white blood cell count was 16,200 cells/mm.

Diagnostic testing included an initial computed tomography (CT) of head that was suggestive of chronic subdural collection showing inappropriate mass effect resulting in effacement of right lateral ventricle with a midline shift of 8 mm to the left (Figures 1 and 2).

With the diagnosis of a subdural collection, the patient was then transferred to the department of neurosurgery, where a right parietal burr hole was done and purulent subdural collection with hemorrhagic tinge approximately 70 ccs was drained. Examination of the purulent discharge demonstrated no organisms on Gram stain or Zein-Nelson's stain, protein content was 5.2 g% and sugar 20 mg%. Cell cytology revealed 30-40 red blood cells per high power field with numerous pus cells.

As scan was suggestive of collection in right frontal sinus, Patient underwent drainage and packing of frontal sinus through transnasal route. On 10<sup>th</sup> post-operative day, the

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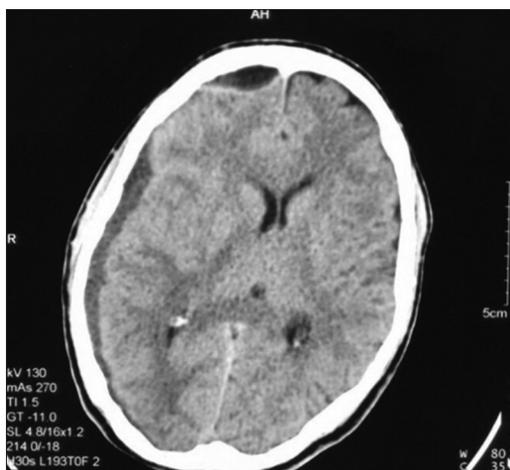


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**Figure 1: Pre-operative plain scan showing right fronto-temporo-parietal subdural collection with inappropriate midline shift**



**Figure 2: Computed tomography scan of head showing rent in posterior wall of frontal sinus**

patient was discharged. The patient was asymptomatic and clinically improved at the time of discharge.

## DISCUSSION

Subdural empyemas are one of the neurosurgical emergencies which require prompt recognition and early management to salvage a good functional neurologic outcome. Some of these lesions progress rapidly and may cause increased intracranial pressure leading patient to coma and if untreated with 24-48 h then will ultimately lead to death.<sup>2,3</sup>

A subdural empyema is a known but rare suppurative complication of the anterior and posterior wall of frontal sinus fracture. Intracranial complications following head injury include subdural empyema, epidural abscess, intracerebral abscess, meningitis, and thrombosis of the cavernous and other dural sinuses. There are two potential

mechanisms for empyema subdural formation following an injury to the frontal sinus. The most common, a retrograde thrombophlebitis occurs via the valveless diploic veins, and seeds the subdural space and then the direct extension can occur from an infected sinus. Frontal sinusitis is the most common culprit in this instance. The close anatomic proximity of the sinus to the subdural space allows for this direct extension. Once the infectious process invades the subdural space, rapid clinical deterioration is expected.<sup>4,6</sup> The subacute course and vague symptoms contribute to the risk of misdiagnosis or delay in diagnosis.<sup>7</sup>

The few common neurologic manifestations are seizures, altered mental status, and hemiparesis, but sometimes focal neurologic deficits may be present if there is an associated intracranial abscess.

Neurologic findings are particularly ominous, but when they are present, rapid neurosurgical intervention is necessary because these symptoms will worsen rapidly.<sup>3</sup> Few of other nonspecific symptoms are nausea, vomiting, personality changes, meningismus, papilledema, cranial nerve palsies, and periorbital edema.<sup>8</sup>

Singh *et al.*<sup>9</sup> found that 37% of patients with subdural empyemas had concomitant extracranial complications. Finding these extracranial complications before neurologic symptoms have developed will improve the likelihood of an uncomplicated outcome.<sup>4,6</sup>

In current era where there is frequent use of CT scan, early diagnosis is much more likely to occur which contributed to the decreased mortality rate and long-term morbidity of suppurative intracranial infections.

CT scan should be done with intravenous contrast if there is a concern for an intracranial infection and if it is found to be negative, then subdural empyema is still considered. In this case, magnetic resonance imaging (MRI) must be done with gadolinium contrast to confirm the diagnosis.

Administration of the third generation of cephalosporin along with metronidazole and vancomycin is given to provide appropriate coverage against streptococci species and *Staphylococcus aureus*.<sup>5,8</sup> Adjunctive seizure prophylaxis is recommended early, as well as seizures may be present in up to 20% of cases.<sup>3,9,10</sup>

Historically, mortality from subdural empyema has been as high as 15-41% even with surgical drainage.<sup>3,7,11</sup>

Certain antimicrobials have found to be significant in lowering the mortality rate, as subdural empyema was universally fatal prior to antibiotic use.

The frequent use of CT and MRI has helped in good way to decrease the mortality rate, with recent studies suggesting a mortality rate ranging between 6% and 15%.<sup>12-15</sup>

## CONCLUSION

Patient of head injury with frontal sinus fracture can present with subdural empyema as a delayed complication.

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# Angiomatous Meningioma Arising in Tonsil: A Rare Tumor at Rare Site

Rajeev K Mishra<sup>1</sup>, Shilpa U Vahikar<sup>2</sup>, Mastraj Singh<sup>3</sup>, G N Lal<sup>4</sup>, Kanchan Shrivastava<sup>5</sup>

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## Abstract

Angiomatous meningioma (AM) is a rare histological variant of meningioma, accounts for 2.1% of all meningioma, accounts for 2.1% of all meningiomas. It is World Health Organization Grade-I histological subtype of meningioma having predominance of blood vessels over that of tumor cells. We report a case of 45-year-old male presented with extradural AM in very unusual site, i.e., rectal tonsil, the great diagnostic difficulty was noticed due to its unusual site. Histopathology of this tumor showed thin walled vascular channels and cells with bland morphology in the background. The diagnosis was confirmed by immunohistochemistry. Tumor cells showed positivity for epithelial membrane antigen, vimentin, CD3<sub>1</sub>, and progesterone. Primary extradural meningioma is a rare entity, extradural AM being rarer still. We present this rare case to highlight the unusual ectopic site of AM and its histopathological features to distinguished it from closely mimicking vascular tumors such as hemangioblastoma and hemangiopericytoma.

**Key words:** Angiomatous meningioma, Extradural, Tonsil

## INTRODUCTION

Neoplasms of the meninges are derived from mesenchymal elements normally present at this site and the most common tumor is meningioma.<sup>1</sup> This distinctive group of tumor accounts for approximately 35% of all primary central nervous system (CNS) neoplasms, 15% of intracranial tumors, and about 25% of intraspinal tumors, with an estimated incidence rate of 6.29/100,000 person - years.<sup>2</sup>

Angiomatous meningioma (AM) is a rare subgroup of meningiomas, constitute 2.1% of all meningiomas.<sup>3</sup> It is World Health Organization (WHO) Grade-I histological subtype of meningioma which has a predominance of blood vessels over that of the tumor cells.<sup>4</sup> Vast majority of these tumors are histologically and clinically benign.<sup>3</sup> Primary extradural meningioma is a far more rare entity.

They have histologic features comparable to those observed in the CNS, including meningothelial, transitional, psammomatous, fibrous, angiomatous, and chordoid variants.<sup>5,6</sup>

They have been reported to occur in a variety of locations including calvarium, orbit, middle ear, paranasal sinuses, nasopharynx, neck, skin, lungs, mediastinum, and retroperitoneum.<sup>7</sup>

## CASE REPORT

We present the case of 45-year-old male patient who came to the ear-nose-throat outpatient department with the complaints of difficulty in swallowing, persistent cough, and cold with a slight change in voice. His complaints began 1-year ago with slowly growing soft reddish brown mass over rectal tonsil. The case underwent tonsillectomy on the lesional side.

Pre-operatively the tumor was highly vascular present within the parenchyma of the tonsil. Complete surgical excision of the rectal tonsil done and the specimen was sent for histopathological examination in 10% buffered

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formalin to histopathology laboratory for routine paraffin sectioning. Hematoxylin and eosin (H and E) stained sections on examination revealed numerous small and medium sized thin walled vascular channels exceeding 50% of the area of the tumor. Most of them are small with hyalinized walls with intervening areas showing oval cells with abundant cytoplasm and vesicular nuclei (Figure 1). Some cells showed vacuolated and clear cytoplasm. The mitotic activity was inconspicuous. Mild degenerative nuclear atypia was present in few cells.

The impression of a vascular lesion was made, and the differential diagnosis included were AM, capillary hemangioblastoma and hemangiopericytoma depending on the prominence of vessels and occasionally non-meningothelial appearance of the tumor cells. However, the diagnosis of AM was confirmed by immunohistochemistry. The tumor cells showed positivity for vimentin (Figure 2), epithelial membrane antigen (EMA) and CD3<sub>1</sub> (Figure 3) and progesterone (Figure 4).

## DISCUSSION

Meningiomas are meningotheial cell neoplasms, typically attached to the inner surface of the dura matter, emerges from meningotheial cells.<sup>8</sup> Most meningiomas are benign and correspond to WHO Grade-I. The WHO classification scheme attempts to predict which tumors are most likely to recur, placing lesions with worrisome histopathological features into Grade-II (atypical) or Grade-III (malignant) categories.<sup>8</sup> This grading system was developed primarily through clinicopathologic correlations using intracranial meningiomas.<sup>9</sup> The current WHO classification has not been applied to a large series of extradural meningiomas. Hence, we discussed the pathology and possibility of developing primary extradural AM in an unusual site.

AM is one the rare subgroup of meningiomas, constitutes 2.1% of all meningiomas.<sup>10</sup> It has the histological and clinical features of benign meningioma in which vascular component exceed 50%.<sup>3</sup> Until now clinicopathologic

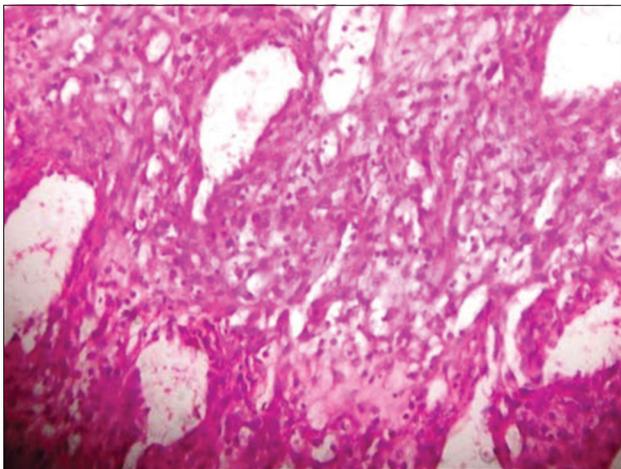


Figure 1: Thin walled dilated vascular channels with intervening areas of meningothelial cells (H and E, x40)

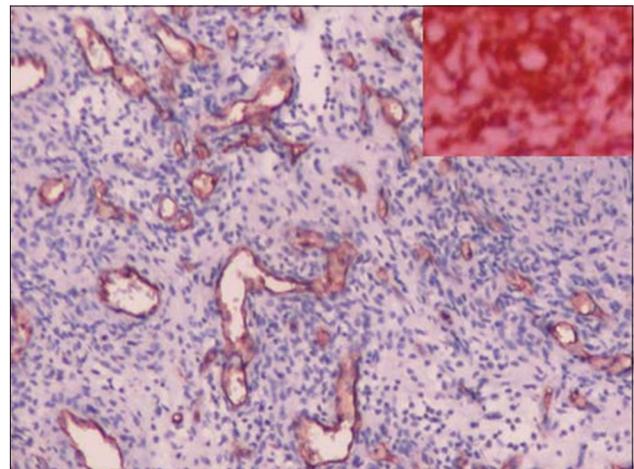


Figure 3: CD3, positivity in blood vessels. Inset - Epithelial membrane antigen positive meningothelial cells

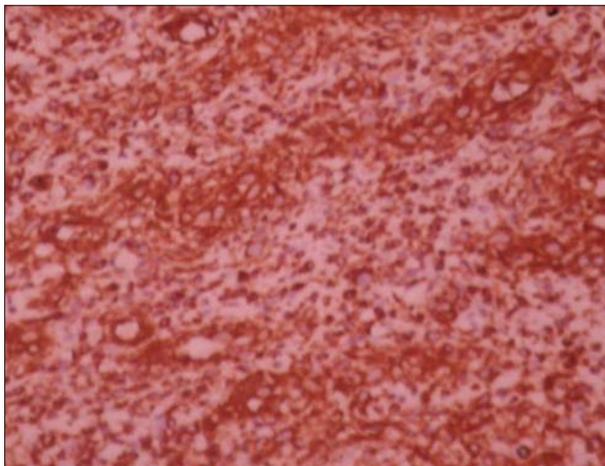


Figure 2: Tumor cells showing positivity for vimentin

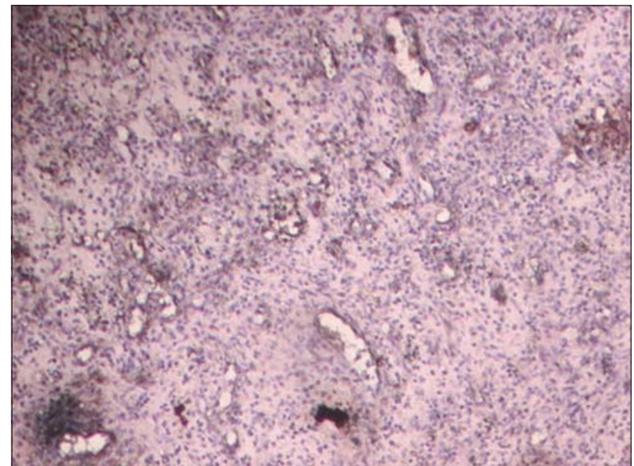


Figure 4: Tumor cells showing positivity for progesterone

characteristics of AM have not been systematically analyzed and studied in detail, first of all by Hasselblatt *et al.* in 2004.<sup>3</sup> They studied 38 cases of AM and confirmed the existence of this rare subgroup of meningioma.

Primary extradural meningiomas account for <2% of all meningiomas and angiomatous extradural meningiomas are rarer than that.<sup>11</sup>

Another large series from Thailand reports that 8% of meningiomas are primary extradural lesions.<sup>12</sup> However, the meaning of extradural is quite variable in the published literature, with some authors including primary intracranial tumors that have extended extra cranially by direct extension or by distant metastasis.<sup>13</sup>

Extradural AM have clinical, histological and immunohistochemical features identical to their CNS counterpart,<sup>7</sup> such as the mean age of onset (AM: 51.8 years and meningioma 49.7 years) 5 years recurrence rate (AM 5.3%, meningioma 7%). Male to female ratio (AM 1:1.4, meningioma 1:2).<sup>3,14,15</sup>

Histologically AM is composed of meningotheial and vascular elements. The vascular component consisted of a multitude of blood channels which ranged from capillary or sinusoidal type to vessels of relatively large caliber with markedly thickened walls.<sup>16</sup>

The intervascular spaces were occupied by sheets of uniform polygonal cells with poorly defined borders of cytoplasm and centrally situated large oval shaped nuclei.<sup>16</sup>

Because of such extremely vascularized nature of this meningioma, previously (it is a generally held) belief that the term angiomatous is more a descriptor than a diagnosis and has no prognostic or any other clinical significance. Furthermore, it has been argued that the presence of this variant might be only justified to represent a niche for highly vascularized meningiomas to distinguish them from vascular tumors like hemangiopericytoma and hemangioblastoma.<sup>3</sup> These three entities share similar clinical features, radiological findings, and histopathological features. Immunohistochemistry can be used to distinguish and to reach the final diagnosis. AM shows similar pattern of immunoreactivity as that of typical meningioma.<sup>1</sup> Tumor cells of AM show positivity for EMA, cytokeratin, vimentin, desmoplakin, and focal positive reaction to antibodies to progesterone.<sup>17</sup> Meningiomas also express steroid hormone receptors, more so for progesterone than estrogen. Lack of progesterone receptor has been correlated with a less favorable clinical outcome.<sup>18</sup>

Further confirmation may be done by elector microscopy. Tumor cells on electron microscopy show cytoplasmic

extensions occupying intervascular spaces formed varying degrees of inter-digitation.<sup>16</sup>

AM had been divided into two pattern according to the diameter of vessels as macrovascular and microvascular by Hasselblatt *et al.* in 2004.<sup>3</sup> According to their study macrovascular pattern shows >50% of vessels having larger size than 30  $\mu\text{m}$  in diameter and microvascular pattern in which shows >50% of vessels were smaller than 30  $\mu\text{m}$  in diameter.<sup>3</sup>

It is the microvascular pattern which can be confused with hemangioblastoma.<sup>1</sup>

Hemangioblastoma is slow growing highly vascular tumor of adults, histologically comprised two main components; stromal cells that are large and vacuolated and abundant vascular cells.<sup>19</sup>

Stromal cells of hemangioblastoma lack endothelial cell markers, such as Von Willebrand factor and CD<sub>34</sub> and do not express endothelium associated adhesion molecules such as CD<sub>31</sub>.<sup>20</sup> Vimentin is the major intermediate filament expressed by stromal cells. Endothelial cells express receptors for platelet derived growth factor and vascular endothelial growth factor.<sup>19</sup>

Hemangiopericytoma is a highly cellular and vascularized mesenchymal tumor composed of irregular cells with ill-defined cytoplasmic margins and staghorn vascular pattern.<sup>1</sup>

Immunohistochemical stains play a vital role in differentiating hemangiopericytoma and hemangioblastoma from AM. Hemangiopericytoma is immunoreactive to vimentin and CD<sub>34</sub> but stains negatively with EMA, which is positive in AM. Even hemangioblastomas fail to stain with EMA and CD<sub>34</sub>, which gives positivity in AM.<sup>19</sup> The importance of differentiating these tumors needs to be emphasized due to the prognostic differences. Because AM belongs to Grade-I meningiomas, it has a favorable prognosis.<sup>8</sup>

The embryonic development of CNS is a complex process involving migration, induction, specialization, differentiation, and remodeling. This process occurs in a system of co-developmental cooperation in coordination with the entire body. Malformations of the CNS are frequently associated with the malformations of the systemic organs and major heterotropias.<sup>21</sup> Our case of primary extradural AM could be the result of these developmental malformations.

Each and every clinician should also consider ectopias and hamartomas in the differential diagnosis of the tumors arising in tonsils.

## CONCLUSION

Although AM is a rare variant of meningioma, it shares similar clinical features and prognosis with benign meningiomas and has some unique clinical, radiological, histopathological, and immunohistochemical features. Primary extradural AM rarely presents with tonsillar involvement hence clinician should consider this entity in the differential diagnosis of tonsillar tumors. It may mimic other vascular neoplasms like hemangioblastoma or hemangiopericytoma creating a diagnostic dilemma which requires immunohistochemistry for final diagnosis.

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# Lateral Neck Pain - Eagle's Syndrome: A Report of Two Cases

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## Abstract

Cervicofacial pain can occur due to elongated styloid process or calcification of stylomandibular ligament or stylohyoid ligament. Other factors also include chronic tonsillitis and tonsillopharyngitis. When the etiology of cervicofacial is elongated styloid process and/or ossification of ligament stylomandibular or stylohyoid it is referred as Eagle syndrome. Here, we are presenting the report of two cases of cervicofacial pain which were due to elongated styloid process and their management. The diagnosis of Eagle syndrome was made and confirm from clinical presentation and radiological investigations. As per present case and the available literature, styloidectomy is the treatment of choice for this condition.

**Key words:** Cervical pain, Eagle syndrome, Styloid process, Tonsillectomy

## INTRODUCTION

Pain in orocervico facial region can occur due to chronic tonsillitis, elongated styloid process (unilateral or bilateral) or ossification of the stylomandibular and stylohyoid ligament. It may exert pressure on various vital structures such as carotid and glossopharyngeal nerve.<sup>1</sup>

Stygalgia was first brought to light in 1937 by Eagle. Hence, it is termed as Eagle syndrome. It is also known by the name Ernest syndrome.<sup>2</sup> The styloid process is a small bony projection of temporal bone, which lies anterior to stylomastoid foramen. The styloid process lies between internal and external carotid arteries, posterior to the tonsillar fossa and lateral to the pharyngeal wall. The styloid process gives attachment to three muscles and two ligaments. The stylohyoid ligament itself extends from the tip of the styloid process to the lesser cornua of the hyoid bone. The stylomandibular ligament extends from the styloid process

to the angle of the mandible. The three muscles include the stylopharyngeus, stylohyoid, and styloglossus. The nerve supply for these muscles comes from glossopharyngeal, facial, and hypoglossal nerves, respectively. The internal jugular vein and the accessory hypoglossal, vagus, and glossopharyngeal nerves are located medial to the styloid process.<sup>3</sup>

The normal styloid process is 2.5-3 cm long as stated by Eagle.<sup>1</sup> Eagle earlier described two types of clinical presentation of stygalgia.

- Classical stylohyoid syndrome
- Stylocarotid syndrome

Eagle considered that only 4% patients with elongated styloid process experienced the orofacial pain meaning not all the elongated styloid processes cause symptoms.

Classical stylohyoid syndrome occurs mostly the following tonsillectomy with localized pain in tonsillar fossa, dysphagia,odynophagia, and hyper salivation, and it is presumed that tightened tonsillectomy scar moving the tip of the elongated styloid process during functional movement causes the orocervico facial pain.<sup>4</sup>

Stylocarotid syndrome occurs due to irritation sympathetic nerve fibers surrounding the internal or external carotid arteries.

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Ossification of the stylohyoid and the stylomandibular ligaments can result in a similar clinical picture. Few authors consider this condition as a stylohyoid syndrome. However, this condition causing cervicofacial pain is further lesser when compared to the ones caused by the elongation of the styloid process itself.<sup>5</sup>

Diagnosis is made with the help of imaging in form of X-rays, and three dimensional computed tomography with which the length and anatomical relations of the elongated styloid process can be assessed and further management can be planned. (Table 1)<sup>6</sup>

Management of Eagle syndrome has been surgical excision of the styloid process and the ossified ligaments under general anesthesia. Other modalities like steroid injection into the scar tissue and drugs to decrease muscle spasms are also used.<sup>7</sup>

Here, we are discussing two cases of Eagle's syndrome with the cause being elongated styloid process and their management.

## CASE REPORTS

### Case 1

A 37-year-old male, came to ENT outpatient department (OPD), Maharani Laxmibai Medical College, Jhansi with a chief complaint of pain in right tonsillar fossa for last 6 months. Pain radiated to the posterior part of the tongue, buccal, and cervical region of the neck.

He was asymptomatic before 6 months when he felt pain on swallowing the food which was moderate in intensity, paroxysmal in nature, and persist for 3-5 min/episode in the beginning, but after sometime pain persist throughout the day and radiated to cervical and temporal region.

He also experiences pain on turning the head on either side. The patients gave a history of tonsillectomy 10 years back and no history of trauma in head and neck region.

On intraoral palpation tenderness was present over tonsillar fossa and posterior part of the tongue.

On radiographic examination, orthopantomogram (OPG) and lateral oblique view of the mandible. Styloid process elongated right side > left styloid process (Figures 1 and 2).

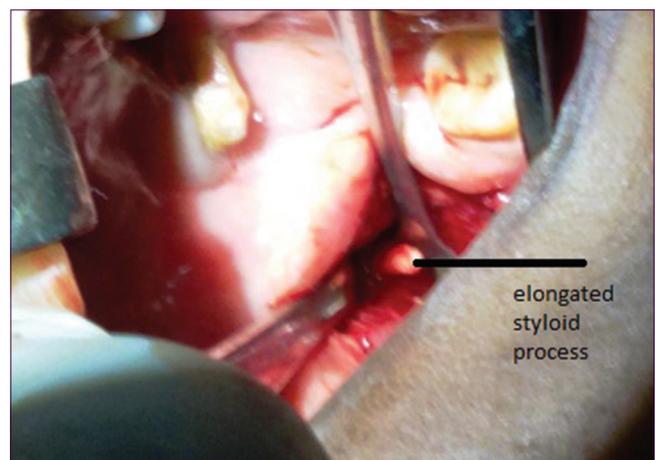
On the basis of history and clinical and radiological examination, the patient was diagnosed as a case of stylalgia (Eagle syndrome) and styloidectomy was done under general anesthesia. After styloidectomy patient got excellent improvement in symptoms (Figure 3).



**Figure 1: Orthopantomogram of the patient showing bilaterally elongated styloid processes more in right than the left**



**Figure 2: The lateral oblique view of mandible showing elongated styloid process with the tip extending up to the angle of mandible**



**Figure 3: Intraoperative image of elongated styloid process**

### Case 2

A 60-year-old male presented in ENT OPD, Maharani Laxmibai Medical College, Jhansi with a chief complaint of pain in the orofacial region for 2 months which started initially on deglutination. The pain was moderate in intensity in the beginning but after sometimes pain

persisted throughout the day and referred to the temporal cervical and posterior part of the tongue.

The pain increases on turning head to either side and referred to the temporal region.

On intraoral examination, Grade-II tonsils were present and on palpation of tonsillar fossa pointed end appears.

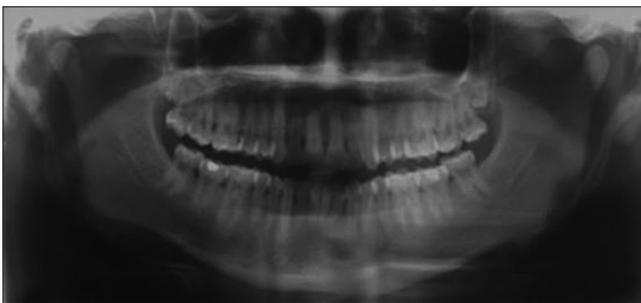
On radiography orthopantomogram elongated styloid process right > left (Figure 4).

Initially, we did conservative management for 3 weeks with antibiotic and analgesic to treat tonsillitis. After 3 weeks of treatment, symptoms did not alleviated, and we planned for surgical management. We did tonsillectomy with styloidectomy and patients got relief from symptoms and became happy.

**DISCUSSION**

The stylohyoid chain consists of the styloid process, the lesser cornu of hyoid and stylohyoid ligament. The stylohyoid complexes are developed from second branchial arch or hyoid arch.<sup>2</sup>

Incidence of osseous metaplasia of stylohyoid ligament varies from 1.4% to 88.7% in asymptomatic individual; but symptomatic ossification of stylohyoid ligament is much rarer <4%.<sup>3</sup>



**Figure 4: Bilateral styloid process**

**Table 1: Morphologic characteristics of styloid process**

Types	Nomenclature	Radiographic appearances
I	Elongated	Uninterrupted integrity of styloid image (>25-28 mm)
II	Pseudo-articulated	The styloid process is joined to the mineralized stylomandibular or stylohyoid ligament by a single pseudoarticulation, usually located superior to inferior border of the mandible
III	Segmented	Short or long continuous portions of the styloid process or uninterrupted segments of mineralized ligament

There are various theories to explain its pathogenesis. According to Steinmann, ossified stylohyoid ligament is congenital anomaly.<sup>4</sup>

Fini *et al.*,<sup>5</sup> reported that past tonsillectomy is related to Eagle syndrome.

Osseous metaplasia of residues of Reichart's cartilage (development, due to surgical trauma or local chronic irritation) resulting in osteitis and periostitis with reactive ossifying metaplasia, a recessive autosomal inheritance, malformation of styloid apparatus associated with malformation of the atlanto-occipital hinge, mucopolysaccharidoses and diffuse idiopathic skeletal hyperostosis, and endocrine disorder in postmenopausal women have all been implicated as pathogenetic factors.<sup>5</sup>

Langlais *et al.*,<sup>6</sup> classified them into; Type I pattern which is an uninterrupted, elongated styloid process. Type II is characterized by the styloid process apparently being joined to the stylohyoid ligament by a single pseudoarticulation giving the appearance of an articulated elongated styloid process, and Type III consisting of interrupted segments of the mineralized ligament, sometimes creating the appearance of multiple pseudoarticulations.

Palesy *et al.*,<sup>7</sup> have hypothesized that since the styloid process lies within the lateral pharyngeal space, a chronic soft-tissue injury there may result in edema resulting in an increase in fascial compartment pressure, thereby affecting neurovascular contents of the space, including the cervical sympathetic chain and glossopharyngeal nerve, through direct mechanoreceptor stimulation. The lingual nerve is intimately related to styloglossus muscle (arising from the styloid process) during its course. Ossified ligament may result in stretched styloglossus and resultantly lingual nerve.<sup>8-10</sup>

A patient with Eagle's syndrome may develop non-specific pain, which may change with head movements at the ear or neck. Additionally, a patient with an elongated styloid process may have referred pain to the jaw joint or upper extremities, or dysphagia or foreign body-like irritation throughout the pharynx.<sup>11,12</sup>

Differential diagnosis includes trigeminal neuralgia, glossopharyngeal neuralgia, sphenopalatine neuralgia, chronic tonsilopharyngitis, temporal arteritis, and temporomandibular joint dysfunction, hyoid bursitis, Sluder's syndrome, etc.

**CONCLUSION**

Treatment options for Eagle syndrome are both surgical and non-surgical. Based on the above-mentioned cases

and their results and already available literature, we find styloidectomy is the treatment of choice for Eagle syndrome.

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# Acute Nitrobenzene Intoxication: A Report of Two Cases

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## Abstract

Nitrobenzene, a pale yellow oily liquid having a bitter almonds odor used as intermediate in the synthesis of aniline dyes, and as a solvent, for the manufacture of cellulose ethers and acetate, as a flavoring agent, as a perfume for soap, and in rubber industry. Cases of self-poisoning with nitrobenzene mixed with alcohol following oral ingestion are reported. Nitrobenzene metabolites are responsible for inducing methemoglobinemia. A patient presented with unconsciousness and acute respiratory distress. Prompt dialysis saved one patient but other patient expired. The aim is to highlight the presentation and the hospital course observed in the case of nitrobenzene poisoning.

**Key words:** Methemoglobinemia, Nitrobenzene, Unconsciousness

## INTRODUCTION

Intentional exposure is a major cause of premature mortality globally and 113914 suicides are recorded annually from India for which a variety of chemicals have been used.<sup>1</sup> Nitrobenzene also known as nitrobenzole or oil of mirbane is a pale yellow oily liquid with an odor of bitter almonds. Nitrobenzene is highly soluble in water readily soluble in organic solvents such as alcohol, ether and benzene, and very soluble in lipids, it serves as an intermediate in the synthesis of aniline dye, solvent, such as paint remover, a flavoring agent, a perfume for soap, and in the rubber industry.<sup>2</sup> The lethal dose is reported to range from 1 to 10 g by different studies.<sup>3,4</sup> Nitrobenzene ingestion primarily causes methemoglobinemia, and this reduces oxygen carrying capacity of red blood cells and also impairs oxygen delivery to the tissues. Clues for diagnosis, includes a history of chemical ingestion, characteristics smell of bitter almonds, persistent cyanosis on oxygen therapy without severe cardiopulmonary disease, and low

arterial oxygen saturation with normal arterial blood gas analysis. Acute poisoning with nitrobenzene has resulted in methemoglobinemia, cyanosis, anemia, and neurological effects including headache, nausea, vertigo, confusion, unconsciousness, apnea, coma, and death.<sup>5</sup> Early and aggressive management of severe poisoning, strongly suspected on clinical grounds may change the outcome of a patient. Here, we are reporting two such cases.

## CASE REPORT

### Case 1

A 17-year-old unconscious male presented to emergency with cyanosis and a grayish-brown hue, labored respiration of 30/min, blood pressure (BP) 60 mm Hg systolic, pulse rate of 150/min, pupils with normal size sluggish reaction, and SPO<sub>2</sub> of 60% on air. His chest was clear. The patient was immediately placed on 100% O<sub>2</sub> by high flow mask. Dopamine support was started at ionotropic dose. There was a history of ingestion of shoe paint remover solvent followed by severe pain in abdomen, nausea, vomiting, and dizziness, after which he was brought to hospital. His arterial blood sample was found to be chocolate brown in color which was suspected to be due to methemoglobinemia. His ABG was suggestive of metabolic acidosis with pH 7.12, PaO<sub>2</sub> 130 mm Hg, PaCO<sub>2</sub> 44 mm Hg, and HCO<sub>3</sub> 13.3 meq/L. Gastric lavage was done via naso-gastric

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tube with sodium bicarbonate, followed by administration of activated charcoal (1 g/kg of 20% suspension) and started with intravenous (IV) fluids. His SPO<sub>2</sub> became 86% but he developed respiratory distress. BP was 90/60 mm Hg on inotropic support. X-ray chest and Electrocardiograms (ECG) were within normal limits. Total leukocyte count (TLC) was 14000/dl with serum bilirubin 1.8 mg/dl (conjugated 1.0, unconjugated 0.80), serum glutamic oxaloacetic transaminase (SGOT) 23, and serum glutamic pyruvic transaminase (SGPT) 21. Urine was dark colored. Serum creatinine and electrolytes were within normal limits. A clinical diagnosis of acute nitrobenzene poisoning with severe methemoglobinemia was made.

Hemodialysis was done and slow IV infusion of ascorbic acid 1 g in 5% dextrose was given thrice a day. After 2 h of dialysis, patient became stable with SPO<sub>2</sub> of 92% and BP of 110/70 mm Hg. His sensorium improved and he became fully conscious after 4 h of dialysis. Gradually, his inotropic support was tapered, and he was discharged on the 5<sup>th</sup> day.

### Case 2

A 21-year-old male was brought to the emergency department with alleged ingestion of some unknown chemical substance. He worked in a printing press. On admission, he was in an unconscious state, not responding to verbal commands and pain. There was history of an episode of vomiting. On examination, the pupils were found dilated, reacting sluggishly to light. Heart rate was 63/min, BP - 76/34 mm Hg, SPO<sub>2</sub> 70%, respiratory rate was 38/min. On examination, cyanosis was present, with marked bluish discoloration of nail bed, fingertips and lower palpebral conjunctiva. Chest auscultation revealed bilateral crepitations. Abdomen was found soft to palpation. The patient was immediately intubated. Inotropic support in the form of dopamine was given. Gastric lavage was done and 100% oxygen was begun. The blood sample withdrawn for investigations revealed severe brownish discoloration with compensated metabolic acidosis. ECG recorded at the time of admission and thereafter was normal with normal chest X-ray. Blood investigation revealed leucocytosis, elevated liver enzymes with mildly deranged renal profile. The urine was dark brown colored. The hemoglobin (Hb) was 6.6 g/dl with TLC 12,600/mm<sup>3</sup>, blood sugar (mg/dl) 121, blood urea (mg/dl) 56, SGOT (U/L) 159, SGPT (U/L) 118, and serum creatinine (mg/dl) 2.1. He was given IV fluids, antibiotics, pantoprazole, and ondansetron. One unit of whole blood was transfused. A clinical diagnosis of acute severe methemoglobinemia of unknown origin was made. From the information provided by the attendants it was derived that the substance consumed was most likely nitrobenzene solution which was used in the printing process as a reducing agent. The patient was put on conservative treatment and hemodialysis was done for 4 h.

The patient failed to respond to treatment administered and expired the next day.

## DISCUSSION

Acute poisonings due to ingestion of nitrobenzene present in consumer products have occurred frequently in the past and are accidental or suicidal.<sup>6</sup> The first report of nitrobenzene poisoning came in 1886<sup>7</sup> and subsequent fatality reports followed.<sup>6,7</sup>

The symptoms which were present were non-specific except for cyanosis which is a typical finding in cases of nitrobenzene poisoning, as methemoglobinemia commonly occurs. This happens when nitrobenzene oxidizes ferrous ion of Hb to ferric state (Fe<sup>3+</sup>), resulting in decreased binding and delivery of oxygen by red blood cells.<sup>8</sup>

Acute intoxication is usually asymptomatic up to the level of 10-15% of methemoglobinemia, showing only cyanosis. Beyond 20% headache, dyspnea, chest pain, tachypnea, and tachycardia develop. At 40-50%, confusion, lethargy, and metabolic acidosis occur leading to coma, seizure, bradycardia, and ventricular arrhythmia. Anemic and G6PD deficient patients suffer more severe symptoms.<sup>3,4</sup>

Nitrobenzene is metabolized to p-nitrophenol and aminophenol and excreted in urine up to 65% and in stools up to 15% after 5 days of ingestion. Liver, stomach, brain, and blood may act as stores and release it gradually.<sup>8</sup>

Symptoms of nitrobenzene ingestion include burning sensation in the mouth, numbness of the tongue, salivation, nausea, vomiting, diarrhea, giddiness, throbbing headache, marked cyanosis, cold and moist skin, weak and rapid pulse, hurried breathing, drowsiness, and coma. The blood is likely to be chocolate-colored due to the presence of methemoglobin. The pupils get constricted at first, and then dilated. Urine becomes dark colored. Convulsions may occur before death. Gastrointestinal toxicity may result in hepatosplenomegaly, jaundice, and altered liver functions. Hematological toxicity may show methemoglobinemia, hemolytic anemia, and Heinz bodies.<sup>9-11</sup>

The fatal dose of nitrobenzene is said to be about fifteen drops, and the MAC in air is about 1 ppm. Death usually occurs within 6-7 h of ingestion.<sup>10</sup>

Chemically induced methemoglobinemia is a life-threatening condition which requires immediate and definitive management. Methemoglobinemia management can be classified into five categories: (1) Reducing toxin's systemic absorption by induction of emesis with ipecac syrup/salt water and facilitating removal of toxin from gastrointestinal

tract by gastric lavage, activated charcoal, and a purgative, (2) reduction of methemoglobin to Hb via reducing agents, (3) treatment of the “functional anemia” (hypoxic state) with hyperbaric oxygen, (4) extracorporeal removal of the chemical, and (5) replacement of methemoglobin with a functional oxygen-carrying pigment.<sup>12</sup>

The definitive treatment of methemoglobinemia is the use of the reducing agent, methylene blue whose action is dependent on production of the reduced form of nicotinamide adenine dinucleotide phosphate (NADPH) by the hexose phosphate shunt and the activity of the enzyme, NADPH-methemoglobin reductase. NADPH is necessary for the reduction of methylene blue to leukomethylene blue, which is responsible for the reduction of methemoglobin into hemoglobin.<sup>11,13</sup> Role of ascorbic acid in reducing methemoglobinemia is controversial as its action is slow and offers little advantage over normal endogenous reduction of methemoglobin. Methylene blue is available as 1% 10 ml vial and for the initial management of methemoglobinemia recommended dose is 1-2 mg/kg to a maximum of 5-7 mg/kg/day. As maximal response to methylene blue usually occurs within 30-60 min; therefore, methemoglobin levels should be monitored and repeat doses of methylene blue should be spaced at least 1 h apart and after evaluating the response to the last dose. G6PD deficiency should be considered if a patient has a negligible initial response to a therapeutic dose of methylene blue.<sup>14</sup> Methemoglobin levels should be continuously monitored as nitrobenzene has the potential for continued methemoglobin production.<sup>12,15</sup> N-acetylcysteine has a controversial role in reducing methemoglobin, so its use not yet approved.<sup>16</sup> Exchange transfusion is indicated in severe cases.<sup>17</sup> Hyperbaric oxygen is reserved for patients who have a methemoglobin level >50% and or those who do not respond to standard treatment.<sup>11</sup>

The patients were unconscious with respiratory distress and hypotension. Due to non-availability of methylene blue specific treatment was not possible at our setup. The patients were treated with supportive therapy. Both patients were posted for dialysis as a desperate measure. The first patient improved, but the second patient failed to respond to the treatment and expired.

## CONCLUSION

Acute methemoglobinemia is usually associated with high mortality. Methylene blue and ascorbic acid are treatment

of choice. Blood exchange transfusion and hyperbaric oxygen therapy are usually reserved for patients who are resistant to standard treatment. Forced diuresis lead to a rapid fall in methemoglobinemia and improve outcome.<sup>3</sup>

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# Bilateral Symmetrical Areolar Vitiligo: A Case Report

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## Abstract

Vitiligo of the areolar region of the breast is an uncommon compared to other parts of the body such as face, hands, and feet; whereas isolated vitiligo of bilateral areolae, without any other associated lesions in the body is even more uncommon. This patient was treated medically, but there was no improvement; instead the depigmentation progressed and involved whole of the areolae on either side or nipple on the right side. This problem can be managed surgically by deepithelialization of areolar skin keeping the dermal element and applying thin split skin graft over the raw area. We report the successful use of this technique in a 30-year-old woman with bilateral areolar vitiligo. Since this is a rare presentation and was successfully managed, we want to report this case.

**Key words:** Deepithelialization, Micrografting, Nipple and areola, Split skin grafting, Vitiligo

## INTRODUCTION

Vitiligo is a relatively common pigmentary disorder affecting any part of the body occurring all over the world. It has no regional or racial predilection. Occurs in 0.5-2% of the population and both sexes are equally affected. This depigmentary disease has significant socio-economic problem apart from physical and cosmetic appearance.

It has a familial tendency and runs in families.<sup>1</sup> The most common sites that are affected are around the eyes (periorbital), around the mouth (perioral), hands and feet.

Even though the exact etiopathogenesis is still not conclusive several theories and hypothesis are offered to explain the defective melanin production. (1) Auto immune<sup>2</sup> and cytotoxic hypothesis resulting in melanocyte dysfunction, (2) neural hypothesis-Neurochemical mediator destroys melanin production, (3) oxidant-antioxidant mechanism.<sup>3</sup> An intermediate or metabolic product of melanin synthesis results in melanocyte destruction, and (4) Intrinsic defect of melanocyte differentiation which impedes melanin production<sup>4</sup>. In spite of the all

hypothesis put forward the exact cause for depigmentation is not established and the combination of factors may be responsible for the cause of vitiligo.

The classification of the lesions is important and has therapeutic and prognostic significance.<sup>5</sup>

The most accepted classification is based on the distribution of the lesions

1. Localized vitiligo-focal, segmental and mucosal
2. Generalized vitiligo-oculo-facial, vulgaris, and mixed
3. Universal vitiligo-complete depigmentation often associated with endocrinal dysfunction.

Body hair in vitiliginous macules may be depigmented and even after treatment there will not be return of pigmentation in the hair.

Areolar vitiligo can be segmental affecting one or both areolae including the nipple. The depigmentation starts as patches and spread centrifugally from center to the periphery. The lesions are rarely solitary, and they give good prognosis with surgical treatment.

## CASE REPORT

A 30-year-old married female having a child presented with a history of depigmentation of both areolae (Figure 1), which started 9 years back and progressively involved whole of areola on either side. The nipple on the right side

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is also depigmented. No history of any other complaints of itching, nipple discharge and pain. The rest of the breasts on either side are normal clinically. Her father is having Vitiligo patches on the legs. The patient had Homeo treatment for the last 5 years without any improvement. She also had treatment by Dermatologist without any benefit.

We performed surgery on both areolae (Figure 2). The epidermal layer of the skin of the areolae was carefully dissected and excised on either side (Figure 3a and b) and

the resultant defect (Figure 4a and b) was covered by thin split skin graft harvested from posterior aspect of the thigh (Figure 5a and b) and pressure dressing was applied. Primary dressing was done on the 5<sup>th</sup> post-operative day and the graft had taken up completely on either side and was discharged. She was on follow-up regularly, and there was no recurrence of the disease even after 3 months (Figure 6). Patient and the family are very happy at the outcome of the operation. However, we advised her to come for follow-up regularly at least for 1 year. The donor area healed well with normal pigmentation (Figure 7). The



Figure 1: Pre-operative



Figure 2: Pre-operative

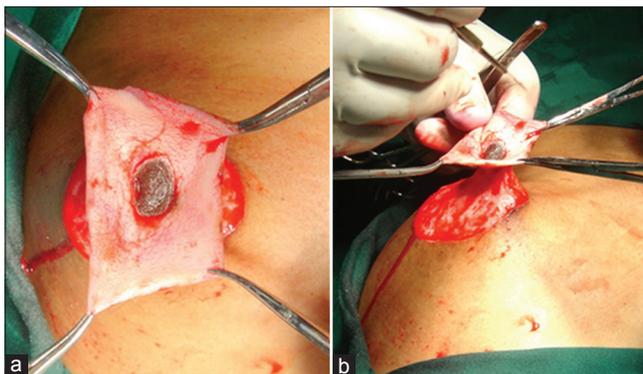


Figure 3: (a) De-epithelialization, (b) Pre-operative-deepithelialization



Figure 4: (a) After excision of lesions both sides, (b) excised specimen both sides

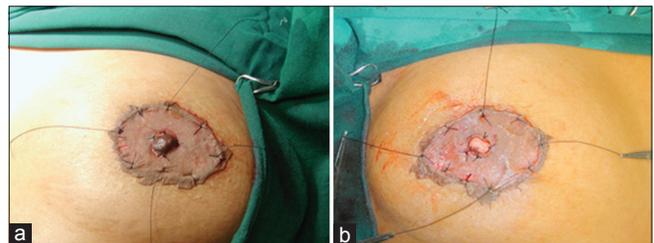


Figure 5: (a) Skin grafting right, (b) skin grafting left



Figure 6: Post-operative - 3 months



**Figure 7: Healed donor area-thigh**

excised areolar skin was sent to the pathology department for histopathological examination.

### Histopathology

“Sections studied from the depigmented bits of both the samples show total loss of melanocytes at the dermoepidermal junction-consistent with Vitiligo.”

### DISCUSSION

Vitiligo is a skin disorder that has more social than medical significance, particularly in dark-skinned people, since it is familial in the majority of cases. Due to retarded melanin formation, there is a loss of pigmentation. The social problems can be so severe that this particular patient was divorced due to this problem after the birth of a child even though she does not have any other lesions on the exposed portion of the body.<sup>6,7</sup>

Vitiligo of isolated areolar region is uncommon, and in this case bilateral symmetrical involvement is extremely unusual.

In vitiligo, surgical therapies must be considered in localized lesions only after proper medical therapy and the lesion is stationary and no more progressive. This patient also used medical treatment, including homeo medicines, but without improvement. Surgical techniques are appropriate only for selected patients who have vitiligo that has been stable over the last 3 years. The various surgical modalities available for treatment of vitiligo are blister grafting, Pinch

grafting, autologous melanocyte transplantation<sup>8</sup> and surgical tattooing.

In our patient, we performed deepithelialization of both areolae sparing the nipple, and not disturbing the ductal system and thin split skin grafting<sup>9</sup> was done which yielded good result. The donor site of the graft also healed well with good pigmentation and Koebner phenomenon was not seen.<sup>10</sup> We are presenting this case because of its rarity and highly satisfactory result, even though we have to follow the patient for a long-term result.

### CONCLUSION

In this presentation, we reviewed the various aspects of vitiligo briefly and presented a case with isolated involvement of both areolae without any other lesions and successfully treated with excision of epidermal layers of affected areolae and replacement with thin split skin grafting which gave very good result when followed after 3 months.

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# Bilateral Primary Adenocarcinoma of Fallopian Tube: A Case Report

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## Abstract

Primary fallopian tube carcinoma (PFTC) is a rare gynecological malignancy. Historically, the first case of PFTC was described by Renaud in 1847. The majority of PFTC are papillary serous adenocarcinoma. Histologically and clinically these tumors resemble malignant epithelial ovarian tumors. It usually arises in old women with a wide range of age with the mean age being about 52.7 years. Pre-operative diagnosis is usually not established in most of the cases. The tumor is usually unilateral and only one in five cases show bilateral tubal involvement. We hereby report a case of bilateral primary adenocarcinoma of the fallopian tube in a 51-year-old woman. This case is being reported owing to its rarity.

**Key words:** Chemotherapy, Dysfunctional uterine bleeding, Malignancy, Metastasis, Papillary adenocarcinoma, Peritoneal, Salpingo-oophorectomy

## INTRODUCTION

Primary carcinoma of the fallopian tube is a rare gynecological malignancy accounts for <2% of all gynecological cancers.<sup>1,2</sup> The pre-operative diagnosis of primary fallopian tube carcinoma (PFTC) is very difficult, especially in earlier stages, as it is not routinely suspected.<sup>3</sup> Most patients are peri-post menopausal. The tumor is usually unilateral and only 20% of the cases show bilateral tubal involvement. The fallopian tubes are frequently involved secondarily from other primary sites, most often the ovaries, endometrium, gastrointestinal tract, or breast.

## CASE REPORT

The 51-year-old female gravida-2, para-2, who attained menopause 4 years earlier, presented with complaints of excessive white vaginal discharge and a backache since 5 months and profuse vaginal bleeding from 3 weeks. On general examination, the patient was cachectic weighing

46 kg. There was mild pallor and no lymphadenopathy. An abdominal examination showed no ascites/organomegaly/any mass. Per speculum examination showed the cervix hyperemic and drawn-up. Cervical OS showed a brownish odorless discharge. On vaginal examination, the exact size of uterus could not be appreciated, and all fornices were free. Laboratory work-up revealed mild anemia with rest routine investigations within normal limits. Trans-abdominal USG showed normal uterus with size measuring 8.5 cm × 5 cm × 3.5 cm with normal endometrium. There is a small to moderate size balloon-shaped, elongated, well-defined, solid density lesion in the right adnexal region measuring 7.5 cm × 3.5 cm × 2 cm. Right ovary could not be separately identified. Left ovary appears normal. No localized or free pelvic/peritoneal collection was seen. Pre-operative endometrial curettage revealed dysfunctional uterine bleeding. The patient underwent trans-abdominal hysterectomy with bilateral salpingo-oophorectomy. Total hysterectomy specimen already cut open measuring 8.5 cm × 5.2 cm × 3.8 cm with both side-tube and ovaries was received (Figure 1). Endometrium was 0.2 cm and myometrium was 3.0 cm thick. Right-sided tubal mass measures 7.5 cm × 3.5 cm × 2 cm. On cut, solid gray-white with areas of hemorrhage and necrosis was noted. The right ovary measures 3 cm × 2 cm, on cut, it was solid gray-white while left-sided tube measures 5 cm × 1.5 cm × 1.0 cm, and on cut, it was solid gray-white with areas of necrosis. Separate left ovary measuring 3 cm × 2 cm already

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punctured. On cut, cystic with the solid area was seen. Under light microscopy, both fallopian tubes showed features of papillary well-differentiated adenocarcinoma as shown in Figure 2(a), in low-power view & in Figure 2(b) whereas right ovary was unremarkable and the left ovary showed simple serous cyst. The patient was advised post-operatively to have a course of combined adjuvant chemotherapy. The patient received six cycles of chemotherapy and was on regular follow-up and well clinically. However, the patient denied for second-look laprotomy.

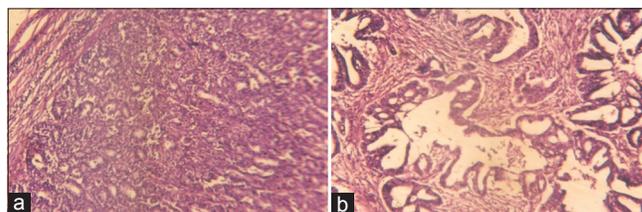
## DISCUSSION

The carcinoma of the fallopian tube is the least common of all gynecological malignancies and accounts for approximately 0.14-1.8% of all female genital tract malignancies. The annual incidence is about 3.6 per million women per year.<sup>4</sup> The primary carcinoma of the fallopian tube is rarer, accounting for about 1% of primary genital tract malignancies.<sup>5</sup> The establishment of the pre-operative diagnosis of tubal carcinoma is rare.<sup>2</sup> Because of its rarity and the non-specific symptoms, the primary diagnosis is rarely made and it is usually misdiagnosed as ovarian carcinoma. A correct diagnosis of PFTC was made pre-operatively in only 4.6% cases in the series of Alvarado-Cabrero *et al.*<sup>1</sup> It usually arises in old woman with a wide range of age and a mean of 52.7 years.<sup>6</sup> 90% of tubal carcinoma have symptoms such as prominent watery vaginal discharge, i.e., hydrops tubac profluens, irregular vaginal bleeding, pelvic mass, and pain.<sup>7</sup> The Latzko's classical triad of symptoms and signs associated with fallopian tube cancer is vaginal discharge, pelvic pain, and mass, which is noted in fewer than 15% of patients.<sup>8</sup> Atypical vaginal bleeding is the most common form of presentation.<sup>9</sup> Symptom of pain and vaginal discharge are more characteristic of tubal inflammation, which is also commonly present. There are no known predisposing factors of PFTC, but it has been found to be associated with nulliparity and infertility, as well as with a pelvic inflammatory disease. Primary carcinoma of the fallopian tube should be included in the differential diagnosis, especially in patients with clinical symptoms of vaginal discharge or abnormal genital bleeding with negative curettage.<sup>4</sup> CA-125 is also a useful marker for diagnosis and follow-up. Grossly, the affected tube resembles a distorted sausage and tends to feel firm. Cut-surface shows a solid or papillary tumor filling the lumen. Microscopic appearance is usually that of an invasive papillary adenocarcinoma of varying degree of differentiation. The close proximity of the fallopian tubes to the ovaries and the uterus sometimes makes it difficult to identify a true primary carcinoma. The criteria for diagnosis of primary tubal carcinoma

should be rigid because the frequency of this tumor is only a tenth of that of direct tubal extensions by uterine or ovarian carcinoma. The diagnostic criteria for PFTC is that tumor should clearly arise from endosalpinx, histologically represents epithelium of tubal mucosa, transition from benign to malignant epithelium should be seen, and ovary and endometrium are normal or have tumor smaller than the one in the tube. By convention, carcinoma extensively involving the endometrium and ovary associated with the tube is regarded as endometrial and ovarian carcinoma respectively. The management of fallopian tube carcinoma is principally the same as that for ovarian cancer. The surgery is the mainstay of the treatment followed by adjuvant combination chemotherapy, that similar to that used for ovarian carcinoma. Taxol and cisplatin combination chemotherapy offers the possibility of long-term control as this combination is today's drug of choice. The prognosis of tubal carcinoma depends more on staging than histological grading. Fallopian tube cancer is staged according to FIGO.<sup>10</sup> The stage of the disease at the time of diagnosis is the most important factor affecting the prognosis. Metastasis to the para-aortic lymph nodes has been documented in 33% of the patients with all stages of disease. More than 50% women present with Stage I or Stage II disease, 40% with Stage



**Figure 1: Gross-specimen of uterus, cervix with both tubes and ovaries: Already cut open dissected right fallopian tube showing grayish white, friable tumor mass and with areas of Hemorrhage and necrosis which is pushing ovary (Rt). Left fallopian tube is swollen at fimbrial end**



**Figure 2: (a) Tumor cells arranged in solid pattern with few areas showing small papillae (H and E x100), (b) tumor cells arranged in papillary pattern with fibrovascular core (H and E x400)**

III and 5-10% with Stage IV disease. A somewhat lower incidence of the advance disease is these women than in those with epithelial ovarian carcinoma, which may be because of earlier occurrence of symptoms, vaginal bleeding or discharge.<sup>11</sup> The survival rate of the tumor studied by Semrad *et al.*<sup>12</sup> shows the 5-year survival rate of about 68-76% disease for Stage I, 27-42% for Stage II and 0-6% for Stage III and IV disease.

## CONCLUSION

Primary carcinoma of the fallopian tube is rare, and its bilateral occurrence is even more rare. PFTC should be taken into account for making the differential diagnosis of a suspicious adrenal mass or tubo-ovarian mass/abscess in all peri- and post-menopausal women as its diagnosis at an early stage provides better prognosis and longer survival.

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