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Original Article

Analytical Study of Impacted Foreign Bodies in Thoracic Surgery and Their Surgical Modalities

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Abstract

Introduction: Foreign bodies (FBs) in the thoracic cavity, its wall or other vital organs in the thorax are not uncommon. Their introduction in the thorax is by various methods. Especially inhalation and ingestion of FBs are common in young children and aged people.

Materials and Methods: Between August 2004 to April 2007, 20 patients had been operated for impacted FBs. All patients were admitted initially in E.N.T Department or Paediatric Department and subsequently referred to Cardiothoracic Surgery Department. All patients underwent routine screening by chest X-ray and computed tomography chest/magnetic resonance imaging whenever needed. The trial attempt of removal by esophagoscopy/bronchoscopy was done by other specialists.

Results: The obtained results are depicted in tabular form Tables 1-3 and Figure 1.

Conclusion: FBs in the aerodigestive tract get impacted due to the disparity in the size and lumen diameter. Commonly non-vegetable FBs tend to get impacted, for example, open safety pin, dollar, and coins fish bones, which needs active surgical intervention 85% are radio-opaque FBs and 15% are radiolucent.

Key words: Bronchus, Foreign body, Oesophagus, Surgical intervention

INTRODUCTION

Foreign bodies (FBs) in the thoracic cavity, its wall or other vital organs in the thorax are not uncommon. Their introduction in the thorax is by various methods. Especially inhalation and ingestion of FBs are common in young children and aged people. Traumatic introduction of FB are more common in the middle age group negligence to intervene immediately, and disparity in size of the FB to the passage where it gets lodged leads to impaction and renders surgery the only option for relief and cure, for example, FB in aerodigestive tract. FB in heart, great vessels and lungs is an emergency to be managed as they embolize and complicate. FB in chest wall and pleural cavity demands immediate surgical attention to prevent complication like infection and subsequent disability.[1-4]

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Although FBs from the aerodigestive tract have been revolutionized by removal using rigid/flexion bronchoscopes/esophagoscopes. The mainstay in surgical when impaction of the FBs occur.[5-8]

In this study, the surgical technique and modalities for the management of various of FBs in thorax has been discussed. All cases were referred cases from other specialties such as E.N.T, pediatric surgery, and general surgery were the first line of management has failed.[8-12]

Aim of the Study

Analytical study of the types of impacted FBs that occurs in thoracic surgical practice and surgical modalities opted in the management of them in various parts of thorax.

Investigations

Radiological findings

X-ray examination of the patient must be performed and should include all the structures from the nasopharynx to the tuberosities of the ischia; otherwise, the FB maybe overlooked.

X-ray should be taken with the neck extended with anteroposterior and lateral views. Anteroposterior views

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in expiration and inspiration should be taken, although these views are sometimes difficult to obtain in very young children. A lateral chest X-ray completes the chest examination.

Screening may also help, but standard X-rays are usually sufficient (Gaffar *et al*., 1982). Computerized tomographic studies may help to show an FB not seen with conventional studies (Berger *et al.,* 1980) isotope scans will demonstrate changes in ventilation and perfusion of lung tissues. These more sophisticated radiological techniques are rarely necessary in obvious cases of inhaled FBs. They should not be ordered if they delay the definitive endoscopic assessment of the patient.

A lateral view of the FB should always be taken. Not only may this reveal some FBs which might otherwise be missed but also on occasion, a child may have ingested two FBs, one smaller than the other which is tucked out of site on the anteroposterior neck/chest radiograph. Objects such as wood, aluminum, glass, plastics, meat and as indicated, dental plates may not be visible without the use of contrast solutions. One helpful sign on the lateral cervical soft tissue film is the presents of a prevertebral gas shadow above an impacted FB in the upper esophagus. This is not frequently overlooked by accident and emergency department staff who presumably are more intend on seeking out evidence of FB itself. Where the history is clear, it is probably not vice to carry out a barium swallow because endoscopy will be complicated by the obscuring presence of the barium.

MATERIALS AND METHODS

Between August 2004 to April 2007, 20 patients had been operated for impacted FBs. M: F - 12:8. Incidence was more common among young (0-30 years), though we had come across old patients also (70-75 years).

All patients were admitted initially in E.N.T Department or Paediatric Department and subsequently referred to cardiothoracic surgery department. All patients underwent routine screening by chest X-ray and computed tomography chest/magnetic resonance imaging whenever needed. Trial attempt of removal by esophagoscopy/bronchoscopy was done by other specialists.

Failure of the above technique landed the patient for surgical exploration by thoracic surgeons. The removal of radio-opaque FB's was done with on table X-ray guidance/c-arm. Removal of radiolucent FB's was done with on table reconfirmation of position with esophagoscopy/bronchoscopy.

RESULTS

The obtained results are depicted in tabular form Tables 1-3 and Figure 1.

DISCUSSION

1. FBs in the aero- digestive tract are more common in younger children and the old.
2. Boys are more frequently involved than girls in the ratio of 2:1.
3. Children have not developed a full posterior dentition and may have immature neuromuscular mechanisms for swallowing and airway protection.
4. Adults – neurologic dysfunction, dental trauma, and aspiration of larger than normal pieces of food, usually associated with alcohol consumption.
5. Unawareness about the seriousness of the problem a negligence leads to varied complication. For example, FB in the esophagus leads to inflammation and retropharyngeal abscess formation and subsequent septicemia.

Table 1: Sex ratio (*n*=20)

Males	Females
12	8

Table 2: Age group affected

Age in years	Sex	
	Males	Females
0-10	3	3
11-20	2	2
21-30	3	2
31-40	1	-
41-50	1	-
51-60	1	-
61-70	1	-
71-80	-	1
81-90	-	-

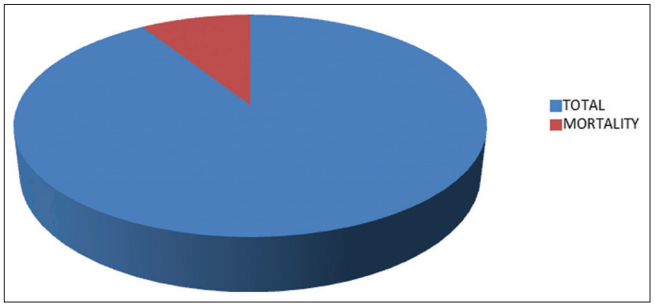

Figure 1: Complication of impacted foreign body. Total (91%), Mortality (9%)

Table 3: Types of foreign bodies

S. No.	Objects	No. of cases presented	Type of foreign bodies
1	Denture (esophagus)	4	Radio opaque
2	Safety pin-open (esophagus)	3	
	Closed	1	
3	Surgical 11 blade (pleural cavity)	1	
4	Bone piece (esophagus)	2	
5	Sewing needle (r.v chamber)	1	
6	Iron rod (chest wall/mediastinum/pleural cavity)	2	
7	Metal cap of soft beverage bottle (esophagus)	1	
8	Coin (esophagus)	2	
9	Plastic nozzle of pen/bead (bronchus)	2	
10	Glass piece (pleural cavity)	1	Radiolucent

6. FB in the bronchus leads to atelectasis initially and later bronchiectasis changes in the lung which may need lobectomy
7. Septicemia was the most common mode of death in patients who, are submitted for surgical exploration of the impacted FB. Second, vascular invasion or erosion of the inflammatory process contributes to the collapse and death of the patient.
8. FB in the pleural cavity iatrogenic (5%) and traumatic (5%) were encountered in adult patients. Empyema with loculation was found in a case 11 blade in the pleural cavity. Prompt recovery was seen on surgical intervention.
9. FB in the myocardial chamber (5%) cardiopulmonary bypass to arrest the heart and retrieve the FB.
10. Three stages of symptoms- initial event of violent paroxysm of coughing, choking, and gagging possibly airway obstruction occurs immediately. Followed by asymptomatic interval due to reflex fatigue. The third stage is complications.
11. Child with recurrent asthma or croup should suspect with FB aspiration.
12. Diagnosis usually delayed more than 1 day in 50% of cases and more than a week in 15% of cases.
13. X-ray posteroanterior and lateral views are needed for the diagnosis.
14. Radiolucent FBs cannot be detected by X-rays. Initially, the object creates a bypass valve which still allows ingress and egress of air. At this stage, radiography results are normal.
15. As edema of the surrounding bronchial wall develops, a check valve is created. On inspiration, the bronchus dilates and permits ingress of air. However, on expiration, the bronchus constricts and contact of the edematous bronchus with the FB block the egress of air. Hence, inspiratory film will be normal but expiratory film will show hyperinflation of the affected lung with shifting of mediastinum to opposite side.
16. Enough edema develops to block ingress and egress of air; a stop valve is created. Obstructive atelectasis is seen radiologically.
17. Treatment of choice is reasonably prompt endoscopic removal under conditions of maximal safety and minimal trauma.
18. Two situations exist, acute emergency, and acute potential airway obstruction.
19. In acute situations, abdominal thrusts can be given, but it is not recommended for children less than 1 year.
20. If obstruction persists despite these efforts, cardiopulmonary resuscitation should be continue until skilled medical personal and appropriate equipment are available to secure the airway.
21. Acute potential airway obstruction cases rigid or flexible endoscopies can be used for retrieval of the FBs.
22. The overall morbidity (4%) and mortality (9%), in this study, are based on the awareness on the side of the patient to seek medical attention at the earliest and timely active surgical intervention.
23. Surgical principles.
24. Cervical esophagus - oblique incision along the left sternomastoid muscle and exploration of esophagus done in visceral space of neck.
25. Thoracic esophagus - Right thoracotomy.
26. Bronchial FB - Prone position of patient and left/right posterolateral thoracotomy as indicated.
27. Myocardium - Cardio-pulmonary bye pass instituted to arrest the heart and remove FB.
28. Others - Chest wall-local incision pleural cavity – right/left anterolateral.

CONCLUSION

1. FBs in the aerodigestive tract get impacted due to the disparity in the size and lumen diameter.
2. Commonly non-vegetable FBs tend to get impacted, for example, open safety pin, dollar, and coins fish bones, which needs active surgical intervention 85% are radio-opaque FBs and 15% are radiolucent.
3. X-ray chest "C" arm, esophagoscopy and bronchoscopy (flexible) are the mainstay of assessment, presurgically to plan an intervention.

Earlier reporting of patients with earliest intervention as discussed above, combined with meticulous post-operative care gave good results with low morbidity and minimal mortality.

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Original Article

Comparison of Silodosin with Tamsulosin in Patients with Symptomatic Benign Prostatic Hyperplasia: A Prospective, Randomized Double-blinded Crossover Drug Trial

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Abstract

Introduction: The treatment option for benign enlargement of prostate gland (benign prostatic hyperplasia) ranges from watchful waiting, medical therapies to various surgical interventions. While various *in vitro* studies have indicated that silodosin has the greatest selectivity for a1 receptors, there are other studies that mention that silodosin is just non inferior to tamsulosin and is an alternative a1-AR blocker.

Materials and Methods: This is a prospective, randomized double-blinded crossover drug trial over a period of 2½ years. 60 patients were enrolled in our study. 30 patients were assigned silodosin preceding group (SPG) and 30 others were assigned to tamsulosin preceding group (TPG). The total duration of the study was 2 months and 1 week (4 weeks initial treatment with 1 week of washout period and 4 weeks of crossover drug for each patient).

Results: International Prostate Symptom Score (IPSS) was the more objective assessment taken into consideration to assess the magnitude of symptomatology and the responses to treatment. Maximal urinary flow rate significantly improved from baseline with both groups in the first treatment period with SPG producing more significant change 9.1-11.3 (P = 0.0005). With silodosin, the quality of life (QOL) is significantly improved (mean of 3.1-2.4 with P = 0.0005) compared to tamsulosin. No patients had a bothersome adverse drug reaction which persuaded for withdrawal of the drug.

Conclusions: Silodosin has significantly improved both storage and voiding symptoms in both the initial period and in the crossover group. Silodosin has scored over tamsulosin in the subgroup analysis of IPSS in nocturia, urgency, max flow rate, and residual urine volume showing an objective improvement. In addition, it has significantly improved the QOL index suggesting that the drug is both objectively and subjectively effective.

Key words: Nocturia, Prostatomegaly, Silodosin, Tamsulosin, Uroflowmetry

INTRODUCTION

Lower urinary tract symptoms (LUTS) constitutes a complex of symptoms comprising either storage (frequency, urgency, and nocturia) or voiding (strain to void, weak stream, intermittency, incomplete emptying) problems. In aging males, even though benign prostatic hyperplasia (BPH) is the most common cause of LUTS, other conditions such as detrusor dysfunction (advanced aging), polyuria, disorders of sleep, and rarely systemic medical illness not related to prostate or bladder should also be considered.

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Patients with LUTS related to BPH should be on periodic monitoring, and at some point, in their lifetime, they may need some form of intervention which could be either medical, MIST (minimally invasive surgical therapy), or

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surgery. Each option is associated with their own balance of risks, benefits, and levels of uncertainty about the long-term outcome. Although surgery is the definitive management for symptomatic BPH, there are potential complications involved both intra- and post-operatively.

The indications for initiating medical treatment in patients with BPH are bothersome LUTS which could affect the patients quality of life (QOL) negatively. The drugs definitely improve the QOL by relieving of symptoms.[1] The features favoring medical treatment are a symptomatic improvement, with less serious and reversible adverse effects when compared to surgery with increased morbidity and sometimes redosurgery may be needed.

The commonly used drugs in the management of BPH are α-1 adrenergic blockers and androgen antagonist (dutasteride and finasteride). The non-selective and short acting α-blockers are not used now due to their requirement of multiple doses in a day and development of tolerance. The subtype selective drugs tamsulosin (1000:1, α1-A:α1-B/α1-D) and silodosin (162:1, α1-A:α1-B) are used now.[2] There are only limited direct comparisons between the two drugs to compare the efficacy. *In vitro* study have indicated Silodosin has the greatest selectivity for a1-AR among all clinically used a-blockers;[3] however, there are lot of controversial studies which says silodosin is just non-inferior to tamsulosin and is an alternative a1-AR blocker.

BPH is a disease that impairs the patient's QOL. There are a less number of guidelines suggesting the clinical profile of the drug. Our study will help to evaluate the clinical profile of the drug in patient perspective to discover which medication they want to continue after completion of the study.

MATERIALS AND METHODS

The study was conducted from August 2013 to January 2016. This is a "prospective randomized double-blinded crossover drug trial with washout period of 1 week." Approval was obtained from the Institutional Ethics Committee, and the study is registered by the Institutional Ethics Committee.

Inclusion and Exclusion Criteria

Ambulatory BPH patients were recruited on the basis of the clinical evaluation with the following inclusion criteria Age: Patients who are aged 50 years and above, the International Prostate Symptom Score (IPSS): 8 and above, QOL index of IPSS: 3 and more and a maximum flow rate of less than 10 ml/s. Patients with neurogenic bladder, bladder neck contracture, stricture urethra, bladder calculi, active urinary tract infection, prostate cancer, long-standing diabetes mellitus, concomitant drug usage such as anticholinergic agents, anti-depressants, anti-anxiety agents, large intravesical extension >2 cm, and large post-void residual urine >100 ml were excluded from the study.

Sample Size

The target sample size was 25 evaluable patients in each group. This was calculated to detect a difference of 4 in total IPSS between groups with 80% power and 0.05 probability of type 1 error, assuming a standard deviation of 5 in total symptom score. Allowing for a 50% dropout rate, this translated to a recruitment target of 60 subjects per group or 120 subjects overall. However, due to various clinical and patient-related reasons, 37 patients were enrolled in each group or over all of 74 subjects. Of them, 11 of them did not come for proper follow-up, and 3 of them withdrew from the study due to personal reasons and are removed from the study. Finally, total of 60 subjects were randomized in a double-blinded 1:1 ratio. Randomization is done using a computer-generated random table designed for 60 patients with 1:1 ratio making 30 patients in each group. Duration of the study is 2 months and one week (4 weeks initial treatment +1 week of washout period +4 weeks of crossover drug for each patient).

All the patients participated in the study were properly explained about the trial. A copy of the participant/patient information sheet typed both in English and Tamil for respective patients is given to the participant for his and our record. They were made to sign the form after understanding the possible risk and benefits involved in the study. Every patient is provided with the primary investigators phone number and was given full rights to contact the primary investigator and to withdraw from the study at any time.

Randomization

The following drugs were used: Capsule tamsulosin 0.4 mg and capsule silodosin 8 mg, respectively. The capsules were removed from their commercial blister strip packaging and repackaged in an empty unicolor coded capsule with sterile precautions. It is kept in air-tight, screw cap containers, and suitably labeled and coded as A group and B group trial medication. To ensure double blinding, repackaging was done with the help of urology clinical instructor and the group identity (Silodosin preceding group [SPG], tamsulosin preceding group [TPG]) is only known to the urology clinical instructor who is involved in the study. Capsule identity was revealed neither to the patients who received the total medication in four installments nor to the primary investigator. Allocation concealment was achieved using the serially numbered, random table with queue basis. The randomization list and the code breaking authority

were retained by a urology clinical instructor not directly interacting with the subjects. Patients will receive either tamsulosin 0.4 mg controlled release or silodosin 8 mg once daily after dinner for 4 weeks followed by 1 week of washout period followed by the crossover drug for 4 weeks. Parameters such as IPSS total score, QOL Score, maximal urinary flow rate (ml/s) residual urine volume (ml) were recorded at the baseline, after 4 weeks and after 8 weeks.

Compliance

By measuring the number of capsules returned at the next study visit, It was deemed to be excellent if <10% of scheduled doses were missed, good if 10- 20% were missed, and fair if 20-30% were missed and poor for any situation worse than fair.

Statistical Analysis

All the data's were compared statistically. The comparison was performed within the groups and between the groups. A baseline value 4th week, 8th week, and 4-8th week was compared. Cure, total responders, and non-responders were analyzed in both the groups. The collected data were analyzed with IBM.SPSS statistics software 23.0 Version. To describe about the data descriptive statistics frequency analysis, percentage analysis were used for categorical variables and the mean and standard deviation (SD) were used for continuous variables. To find the significant difference between the bivariate samples in independent groups, the unpaired sample *t*-test was used. For the multivariate analysis, the one-way ANOVA with Tukey's *post-hoc* test was used and for repeated measures the repeated measures of ANOVA with adjustment for multiple comparisons to control the Type I error, the Bonferroni test was used. To find the significance in categorical data, Chi-square test was used. In all the above statistical tools, the $P = 0.05$ is considered as statistically significant level.

RESULTS

A total of 60 patients were enrolled in our study, and of them, 30 patients were assigned to silodosin as SPG and 30 patients were assigned to tamsulosin as TPG. Baseline parameters of age, prostate volume, total IPSS score, and its subscores, QOL score; Table 1 describes the comparison of the maximal urinary flow rate and residual urinary volume of both the groups recorded at day zero. The results are not significant between both the groups. Following 4 weeks of the drug intake, both the groups were compared again. The response evaluation at 4th week and the comparison from baseline to 4th week of the drug administration are summarized in Table 2. In SPG, the total number of cured patients (IPSS score <8) at initial drug administration were 2 (6.7%; $N = 30$), total number of 28 patients out of 30 (*n*) responded (reduction of IPSS to less than 4 points) to initial drug administration which is 93.3% of total response. In TPG, total number of responders to the initial treatment with tamsulosin is 21 (70%; $N = 30$) and there were 9 (30%; $N = 30$) non-responders (IPSS score not reduced to less the 4 points). There are no cure rates observed in TPG. Figure 1 illustrates 4th-week comparison of both the groups from baseline.

IPSS score was the more objective assessment taken into consideration to assess the magnitude of symptomatology and the responses to treatment. The changes in the objective and subjective parameters in each group are illustrated in Table 3. The total score was significantly improved from the baseline after administration of the drug in both groups. Table 4 illustrates the overall mean reduction of IPSS in SPG is 8.73 (SD = 3.4) compared to 5.93 (SD = 3.5) IPSS reduction in the TPG. Figure 2 depicts the comparison from the baseline, of both groups at the end of 4 weeks of treatment.

Sub Group Symptoms

Comparison of initial treatment period in TPG shows significant changes in both voiding and storage symptoms,

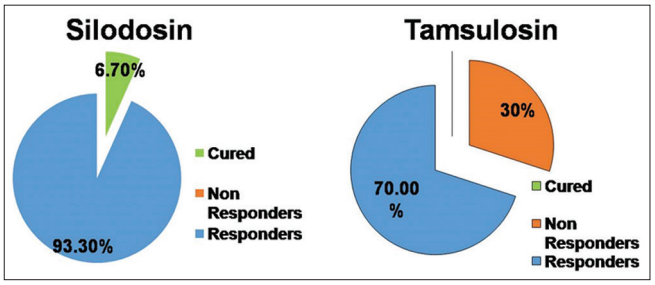

Figure 1: Overall comparison of both the groups from baseline at 4 weeks of drug administration

Table 1: Baseline parameters of all patients in both groups

Parameters	SPG	*N*	TPG	*N*	*P* value
Age (years)	60.5 (SD 6.4)	30	62.8 (SD 4.4)	30	NS
Prostate volume (ml)	39.9 (SD 8.5)	30	37.8 (SD 8.9)	30	NS
IPSS total score	20.6 (SD 2.6)	30	21.6 (SD 3.4)	30	NS
QOL score	3.9 (SD 1.0)	30	3.8 (SD 1.1)	30	NS
Maximal urinary flow rate (ml/s)	9.1 (SD 0.8)	30	9.1 (SD 0.6)	30	NS
Residual urine volume (ml)	89.2 (SD8.8)	30	90.7 (SD 7.8)	30	NS

SD: Standard deviation, SPG: Silodosin preceding group, TPG: Tamsulosin preceding group, QOL: Quality of life, IPSS: International Prostate Symptom Score, NS: Not significant

but of the subgroup parameters-incomplete emptying, nocturia does not show significant improvement. Subgroup analysis of SPG in initial treatment period shows significant changes in both storage and voiding symptoms and in all subgroup parameters (Figure 3).

Maximal Urinary Flow Rate

Maximal urinary flow rate was significantly improved from baseline with both groups in the first treatment period with SPG producing more significant change 9.1-11.3 ($P = 0.0005$) compared to 9.1-10.7 in TPG (0.0090) (Table 3).

Residual Urine Volume

Both the groups showed significant reduction in residual urine volume. The reduction in SPG was 44.3 ml (from 89.2-44.9), with $P = 0.0005$ and in TPG was 30.8 ml (from 90.7 to 59.9), with $P = 0.0005$. Figure 4 illustrates the change in residual urine at 4th week of drug administration.

Response Evaluation at 8th Week at the End of Crossover Period

IPSS

In TPG, silodosin produced a significant further reduction in the IPSS from 15.7 to 12.9 (difference of 2.8, mean with SD 2.4) which tamsulosin has not improved in the initial period of treatment. In SPG, tamsulosin also shows reduction in overall IPSS from 11.8 to 10.3 (difference of 1.5, mean with SD 2.59). The difference in the overall reduction of IPSS Score was high with crossover to SPG (difference −1.30) compared to TPG which is statistically significant ($P = 0.053$) with −2.616 versus 0.016 at 95% confidence interval goes in favor of silodosin (Table 5).

Sub Score Analysis at Cross-over Period

In 4th versus 8th week, silodosin seems to show improvement over tamsulosin in voiding symptoms (mean 6.5-5.7 with $P = 0.01$) and storage symptoms (mean 6.0-1.6 with

Table 2: Comparison from baseline to 4th week of the drug administration

IPSS response	Groups		Total
	SPG	TPG	
Cured			
Count	2	0	2
% within groups	6.7	0.0	3.3
Non-responders			
Count	0	9	9
% within groups	0.0	30.0	15.0
Responders			
Count	28	21	49
% within groups	93.3	70.0	81.7
Total			
Count	30	30	60
% within groups	100.0	100.0	100.0

SPG: Silodosin preceding group, TPG: Tamsulosin preceding group, IPSS: International Prostate Symptom Score

Table 3: Changes observed in the objective and subjective parameters in each group

Parameters studies	Groups	Mean±SD			0 versus 4th week	0 versus 8th week	4th versus 8th week
		Baseline	4th week	8th week			
IPSS score	SPG	20.6±2.6	11.8±2.8	10.3±1.9	0.0005	0.0005	0.01
	TPG	21.6±3.4	15.7±2.1	12.9±2.6	0.0005	0.0005	0.0005
Voiding symptoms	SPG	10.1±2.1	5.6±2.3	4.8±1.8	0.0005	0.0005	0.02
	TPG	10.7±2.4	6.5±1.6	5.7±1.6	0.0005	0.0005	0.01
Storage symptoms	SPG	6.6±1.7	3.8±1.3	3.7±1.4	0.0005	0.0005	NS
	TPG	7.5±1.0	6.0±1.3	4.8±1.6	0.0005	0.0005	0.00
Incomplete emptying	SPG	2.4±1.2	1.3±0.6	1.2±0.6	0.0005	NS	NS
	TPG	2.6±1.3	1.7±0.7	1.5±0.6	NS	0.04	NS
Frequency	SPG	2.3±1.1	1.7±0.6	1.6±0.6	0.0100	0.0010	NS
	TPG	2.8±1.2	1.9±0.6	1.6±0.7	0.0040	0.0005	NS
Intermittency	SPG	2.2±1.2	1.3±0.7	1.2±0.6	0.0005	0.0005	NS
	TPG	2.5±1.4	1.8±0.8	1.6±0.9	0.0080	0.0120	NS
Urgency	SPG	1.9±0.9	0.9±0.6	0.9±0.6	0.0005	0.0005	NS
	TPG	2.2±0.9	1.5±0.9	1.2±0.8	0.0500	0.0010	0.05
Weak stream	SPG	3.3±1.4	2.2±1.4	2.0±1.4	0.0030	0.0010	NS
	TPG	3.4±1.2	2.0±0.9	1.8±0.8	0.0005	0.0005	NS
Straining	SPG	2.4±1.0	0.7±1.0	0.4±0.6	0.0005	0.0005	NS
	TPG	2.3±1.1	1.0±0.9	0.9±0.8	0.0005	0.0005	NS
Nocturia	SPG	2.2±1.4	1.2±1.0	1.2±0.9	0.0050	NS	NS
	TPG	2.4±1.4	2.1±0.7	1.9±0.7	NS	0.0040	0.04
QOL score	SPG	3.9±1.0	2.5±1.0	2.4±0.9	0.0005	0.0005	NS
	TPG	3.8±1.1	3.1±0.7	2.4±0.7	0.0090	0.0005	0.0005
Max.flow rate	SPG	9.1±0.8	11.3±2.8	10.2±2.3	0.0005	NS	NS
	TPG	9.1±0.6	10.7±2.2	11.4±2.2	0.0090	0.0005	0.0005
Residual urine volume	SPG	89.2±8.8	44.9±16.7	39.2±14.6	0.0005	0.0005	0.00
	TPG	90.7±7.8	59.9±14.9	42.8±14.3	0.0005	0.0005	0.0005

SD: Standard deviation, SPG: Silodosin preceding group, TPG: Tamsulosin preceding group, QOL: Quality of life, IPSS: International Prostate Symptom Score, NS: Not significant

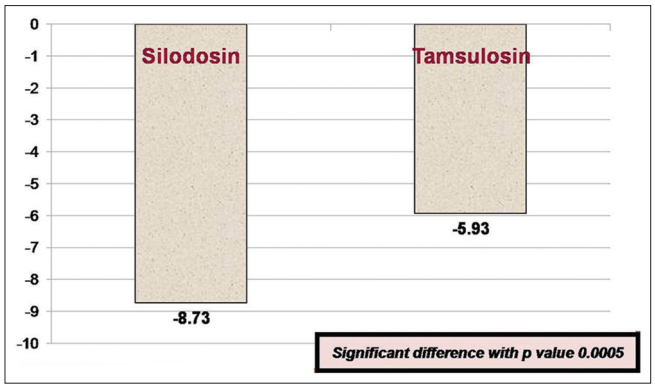

Figure 2: Comparison of International Prostate Symptom Score of both groups from base line at 4 weeks

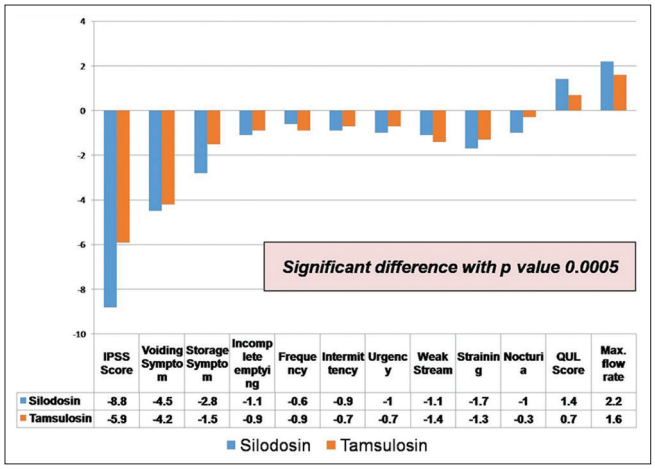

Figure 3: Change from baseline of International Prostate Symptom Score during the first treatment period

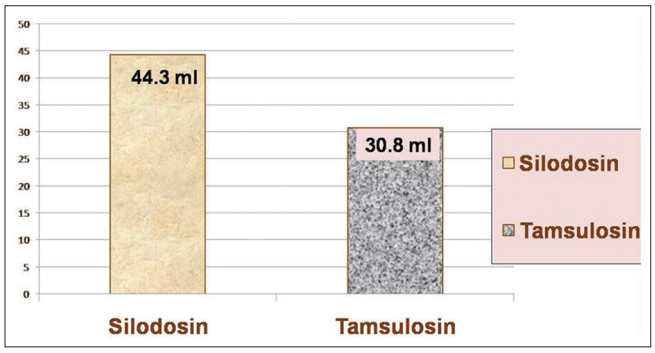

Figure 4: Changes in residual urine levels at 4 weeks

P = 0.001). The analysis shows a further improvement with sub-scores of silodosin in urgency (mean of 1.5-1.2 with P value of 0.05) and nocturia (2.1-1.9 with P value of 0.04). The changes from 4th week of international prostate symptom subscore to cross over treatment are depicted in Figure 5.

Maximal Urinary Flow Rate

It was showing significant improvement from baseline with both silodosin and tamsulosin in the first treatment period

Table 4: The overall mean reduction of IPSS in SPG is 8.73 (SD 3.4) compared to 5.93 (SD 3.5) IPSS reduction in the TPG

IPSS reduction	Mean±SD	*P* value	Mean difference	95% CI	
Diff. 4th versus baseline					
SPG	8.73±3.473	0.0005	2.800	0.979	4.621
TPG	5.93±3.571				

SPG: Silodosin preceding group, TPG: Tamsulosin preceding group, IPSS: International Prostate Symptom Score, CI: Confidence interval, SD: Standard deviation

Table 5: Change in IPSS at the end of 4th and crossover period

IPSS difference	Mean±SD	*P* value	Mean difference	95% CI	
Diff. 04					
SPG	8.73±3.473	0.0005	2.800	0.979	4.621
TPG	5.93±3.571				
Diff. at crossover					
SPG	1.50±2.596	0.053	−1.300	−2.616	0.016
TPG	2.80±2.497				

SPG: Silodosin preceding group, TPG: Tamsulosin preceding group, IPSS: International Prostate Symptom Score, CI: Confidence interval

with silodosin producing more significant change 9.1-11.3 compared to 9.1-10.7 in tamsulosin. However, similarly, this result was also evident in the crossover period with further improvement in the maximal urinary flow rate in silodosin group, TPG at 8th week which is 10.7-11.4 with P = 00005, whereas in SPG, tamsulosin does not produce any improvement in flow rate 11.3-10.2 (−1.1).

Residual Urine Volume

The change in the residual urine volume in SPG is 44.9 with SD of 16.7 compared to baseline of 89.2 with SD of 8.8 and with TPG it is 59.9 with SD of 14.9 compared to baseline of 90.7 (SD 7.8) in the initial treatment period. Both the drugs produced a significant response in the initial treatment period, but silodosin showed a statistical significant in the crossover group with a change of 42.8 (SD 14.3) from 59.9 (P = 0.0005). Figure 6 illustrates the changes in residual urine at the end of crossover group.

QOL

With silodosin, the QOL is significantly improved (mean of 3.9-2.5 with P = 0.0005) compared to tamsulosin (mean of 3.8-3.1 with P = 0.0090) in the initial treatment period, which is considered to be statistically significant. However, tamsulosin did not show any significant difference in the crossover group.

Adverse Drug Reaction

The adverse drug reactions were noted in 22 patients of 60 in SPG and 25 patients of 60 in TPG. Table 6 illustrates the list of all adverse reactions observed during the study.

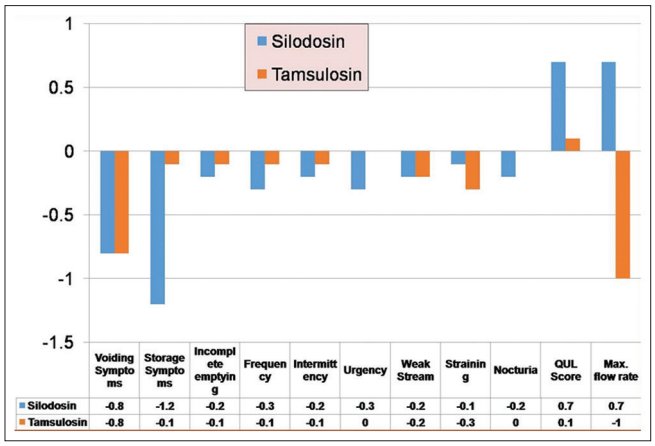

Figure 5: Change from 4th week of International Prostate Symptom Score subscore to cross over treatment

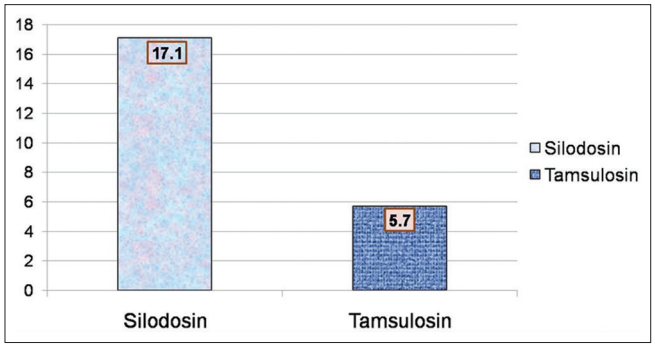

Figure 6: Changes in residual urine levels at the end of crossover group

Frequently observed adverse drug reaction to SPG was ejaculatory disorder in 17 of 60 patients. In TPG, adverse drug reaction was noted in 25 patients of 60; the most pronounced reaction was dizziness 16 of 60 patients. All of these adverse drug reactions were mild and resolved or were relieved in all patients with continued administration or dose reduction or withdrawal. No patients had a bothersome adverse drug reaction which persuaded for withdrawal of the drug.

DISCUSSION

The optimal initial treatment for patients with moderate or severe LUTS caused by BPH involves the use of a-blockers which acts mainly on dynamic component of obstruction (smooth muscle tone).[4] In men with large glands, 5a-reductase inhibitors such as finasteride and dutasteride may be beneficial that acts on the static component of obstruction.[4]

Various studies have confirmed that BPH is a progressive disease causing an average annual increase of the IPSS by 0.18 points, 2% annual reduction of the maximum flow rate (Q-max), and a median increase of prostate size by

Table 6: Adverse drug reaction: Adverse drug reaction was noted in 22 patients of 60 in SPG and 25 patients of 30 in TPG

Effects	SPG	TPG
Ejaculatory disorder	17	5
Dizziness	2	16
Nasal congestion	1	0
Diarrhea	2	0
Arthralgia	0	0
Orthostatic hypotension	0	4
Total	22/60	25/60

SPG: Silodosin preceding group, TPG: Tamsulosin preceding group

1.9% annually.[5] The uroselective a-blockers tamsulosin and silodosin are the preferred drugs for LUTS related to BPH due to their preferential action over α-1A receptor that is predominantly present in prostate and bladder base. Moreover, these drugs cause no significant change in blood pressure or heart rate at doses which are used for treating LUTS.[6]

There are very few head to head comparison studies, comparing the efficacy of these two a-blockers. A thorough PubMed search was carried out with keywords such as tamsulosin, silodosin, and their comparison in BPH that revealed various studies claiming mixed results. Yamanishi *et al.*, in his study on 194 male patients, compared the efficacy of silodosin and tamsulosin after 12 months of drug administration and concluded that both silodosin and tamsulosin improved LUTS and urinary flow rate significantly in patients with BPH.[7] Their efficacies were not significantly different. A randomized crossover study Watanabe *et al.* comparing patient preference for tamsulosin and silodosin in 84 (n = 42 per group) Japanese patients over 4 weeks for each drug concluded that patients preferred tamsulosin over silodosin.[8] A prospective randomized crossover comparative study of 46 patients by Yokahama *et al.* with 23 patients in each group of tamsulosin and silodosin found that both drugs have similar efficacy.[9]

A randomized crossover comparison of the short-term efficacy and safety of half dose of silodosin for 4 weeks and full dose of tamsulosin 4 weeks was done by Takeshita *et al.* in 34 Japanese men over 50 years and an IPSS of more than 8. He concluded that both half doses silodosin and tamsulosin are equally efficacious.[10] Since various studies had produced divergent results, we compared the efficacy and safety of 0.4 mg of tamsulosin and 8 mg silodosin. Our results have clearly shown that silodosin is safe and more efficacious in comparison to tamsulosin.

Primary Outcome Measure – IPSS

Various studies have compared the IPSS after the use of silodosin and tamsulosin and conflicting reports have

been arrived at. Multicentric randomized controlled trial (RCT) conducted by Chapple *et al.* found that responder rates according to total IPSS were significantly higher with silodosin (66.8%) when compared to tamsulosin (65.4%) than with placebo (50.8%) and concluded that the overall efficacy of silodosin is not inferior to tamsulosin.[11]

The trial conducted by Yu *et al.* found that, out of 170 (81.3%) study completed patients, 86.2% in the silodosin group versus 81.9% in the tamsulosin group achieved a ≥25% decrease in IPSS ($P = 0.53$). The mean difference in IPSS change from baseline was −0.60 (95% confidence interval −2.15 to −0.95) (silodosin minus tamsulosin) showed silodosin was non-inferior to tamsulosin.[12]

A phase III randomized, placebo-controlled, double-blind study Kawabe *et al.* in 457 patients who were randomized (silodosin 176, tamsulosin 192 and placebo 89) to receive silodosin 4 mg twice daily, tamsulosin 0.2 mg once daily, or placebo, for 12 weeks showed changes in the total IPSS from the baseline in the silodosin, tamsulosin, and placebo groups as −8.3, −6.8, and −5.3, respectively. A decrease in IPSS on patients with silodosin group started from 1 week compared with the placebo.[13] Marks *et al.* from a pooled analysis of two RCTs in the United States concluded the use of silodosin helps in rapid improvement in LUTS when compared to placebo and at 12-week IPSS, and subscores difference was increased.[14]

A randomized controlled trial done by Pande *et al.* with the evaluation of silodosin in comparison to tamsulosin in 53 subjects reported that the final IPSS scores at 12 weeks were significantly less than the baseline for both drugs and scores remained comparable concluding both are equally efficacious.[15] Another study comparing short-term effects of crossover treatment with silodosin and tamsulosin by Miyakita *et al.* showed that even though in the first-treatment period both drugs significantly improved the IPSS score, the improvement by silodosin was significantly superior to that by tamsulosin.[16]

In our study, out of 30 patients in SPG following 4 weeks of the drug intake, number of cured patients (IPSS score <8) were 2 (6.7%; $N = 30$)and 28 patients were responded (reduction of IPSS to <4 points) which is 93.3% of total response. In TPG, number of responders with tamsulosin were 21 (70%; $N = 30$) and 9 were (30%; $N = 30$) non-responders (IPSS score not reduced to less the 4 points). There are no cure rates observed in TPG.

Even though the total score significantly improved from the baseline after administration of the drug in both the groups. the overall mean reduction of IPSS in SPG was 8.73 compared to 5.93 in the TPG. At the end of crossover period in TPG, silodosin produced a significant further reduction in the IPSS from 15.7 to 12.9, whereas in SPG tamsulosin also shows reduction in overall IPSS from 11.8 to 10.3. The difference in the overall reduction of IPSS at both 4th week and at crossover period suggest silodosin to be more efficacious.

Secondary Outcome Measures

Sub group symptoms

Crossover treatment with silodosin and tamsulosin by Miyakita *et al.*[16] revealed that silodosin caused a significant improvement in nocturia and straining to void in the first and crossover period. In our study, at the end of 4th week, even though tamsulosin shows significant improvement in both voiding and storage symptoms, incomplete emptying, nocturia does not show any improvement, whereas silodosin shows significant changes in both storage and voiding symptoms and in all subgroup parameters also. At the end of crossover period, silodosin showed improvement in urgency and nocturia over tamsulosin, thus concluding that silodosin showed a better improvement in bothersome storage LUTS.

The reasons that α-1A-receptor blockers improve both storage and voiding symptoms may be that bladder outlet obstruction is relieved, and this reduces detrusor overactivity (caused by obstruction). A reduction in the prostatic urethral tension may also cause reduction in detrusor overactivity.[17] Another possible mechanism of bladder outlet obstruction causing detrusor overactivity is that ischemia and reperfusion caused by obstruction leading to overactive bladder.[18] In the small arteries of the bladder, there is an abundance of α-1A-AR and α-1A-AR blockers may increase blood flow to the bladder causing reduced detrusor overactivity.[19,20]

Maximal urinary flow rate (Qmax)

Chapple *et al.* observed an increase in Qmax in all groups, where the adjusted mean change was 3.77 mL/s for silodosin, 3.53 mL/s for tamsulosin, and 2.93 mL/s for placebo. He concluded that the changes were not statistically significant between both drugs.[11] Yu *et al.* also reported that the changes in mean Qmax were comparable between both drugs and were not statistically different.[12] In the crossover study by Miyakita *et al.* even though Qmax increased in both groups initially after 4 weeks, at the end of crossover no significant improvement occurred in both groups.[16] In our study, Qmax showed a significant improvement in both groups with silodosin producing more significant change 9.1-11.3 ($P = 0.0005$).

Residual urine volume

Miyakita *et al.,* at the end of 4th week of the study, showed a reduction in residual urine noted only with silodosin, but

not with tamsulosin at 4th week or to both after crossover trial.[16] In our study, at the end of 4th week, both the groups showed a significant reduction in residual urine volume. However, silodosin showed a statistically significant improvement in the crossover group with a change of 42.8 ml from 59.9 ml ($P = 0.0005$) compared to tamsulosin of 39.2 from 44.9 ml.

QOL

The QOL as per Pande *et al.* was comparable between silodosin and tamsulosin groups at 12-week.[15] Miyakita *et al.* concluded that QOL score significantly improved in both at initial and crossover the period with silodosin.[16] Kawabe *et al.* also reported a significant improvement of the QOL score in patients with silodosin in relative to placebo.[13] In our study with silodosin, the QOL is significantly improved (mean of 3.9-2.5 with $P = 0.0005$) compared to tamsulosin in the initial treatment period and also at the crossover period. However, tamsulosin did not show any significant difference in the crossover group.

Adverse drug reaction

The most common adverse effects according to Pande *et al.* was retrograde ejaculation seen in 3 out of 26 subjects with silodosin. Dizziness or postural hypotension was found in 3 subjects out of 27 in patients who received tamsulosin.[15] In a phase III double-blind study, 28% of the patients on silodosin at 8 mg once-daily developed ejaculatory disorders (28.1% for silodosin versus 0.9% for placebo), followed by dizziness, diarrhea, orthostatic hypotension headache, nasopharyngitis, and nasal congestion in decreasing order of frequency.[14] About 2.8% of patients on silodosin discontinued it because of retrograde ejaculation. The reason for ejaculatory disorders could be attributed to either retrograde ejaculation due to a-receptor blockade on bladder neck contraction, or due to inhibition of the contraction of vas and seminal vesicle.[21] According to Kawabe *et al.* the rates of adverse events in the silodosin, tamsulosin, and placebo groups were 88.6%, 82.3%, and 71.6%, respectively, and the most common event in the silodosin group was abnormal ejaculation when compared to tamsulosin group (22.3% vs. 1.6%).[13] In our study, adverse drug reactions were noted in 22 patients of 60 in SPG and 25 patients of 60 in TPG. The frequently observed adverse drug reaction to SPG was ejaculatory disorder in 17 of 60 patients. In TPG, adverse drug reaction was noted in 25 out of 60, and the most pronounced reaction was dizziness in 16 patients. All the adverse drug reactions excluding ejaculatory disorder were minimal and were relieved with continued administration or dose reduction or after withdrawal of the drug. No patients had a bothersome adverse drug reaction which persuaded for withdrawal of the drug.

CONCLUSIONS

In this study, silodosin has significantly improved both storage and voiding symptoms in both the initial period and in the crossover group. Silodosin has scored over tamsulosin in the sub group analysis of IPSS in nocturia, urgency, max flow rate, and residual urine volume showing an objective improvement. In addition, it has significantly improved the QOL index suggesting that the drug is both objectively and subjectively effective. The incidence of ejaculatory disorder was higher in the silodosin than in the tamsulosin. All other adverse drug reactions were mild seems to be not much bothersome. These reactions were reversible when the drug is discontinued. Considering all the above, it is clearly evident that silodosin a highly selective α1-A-adrenoceptor antagonist exhibited excellent efficacy in improving subjective symptoms regardless of period of administration, and appears to improve QOL in patients with BPH/LUTS.

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Original Article

Cutaneous Manifestations of Systemic Lupus Erythematosus - A Retrospective Study

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Abstract

Background: Lupus erythematosus is a systemic autoimmune disorder with polyclonal B cell activation resulting from interplay of genetic, environmental, and hormonal elements. Heterogenous clinical expression is considered a continuum or spectrum extending from limited cutaneous disorder to life-threatening systemic disease process.

Aims: The aim of the present study is to find the age and sex incidence, precipitating or exacerbating factors, clinical features, cutaneous manifestation of systemic lupus erythematosus (SLE) and relationship with systemic manifestations if any, laboratory profile and its relationship with disease activity.

Materials and Methods: A retrospective study was carried out over 1 year from May 2015 to April 2016. A total of 110 SLE patient's details who attended our hospital were collected from the medical records.

Results: The most common age group affected was between 2nd and 3rd decades. Female preponderance with a female to male ratio of 9:1. Photosensitivity was the most common precipitating and exacerbating factor followed by infections, mental stress, and pregnancy. The most common symptoms were fever, easy fatiguability, diffuse hair loss, and arthralgia. The most common disease specific skin lesion was malar rash and nonspecific but disease related skin disease was diffuse hair loss. Musculoskeletal system was the most common system involved. Renal failure was the most common cause of death. Malar rash and oral ulcer had a parallel course with disease activity. Antinuclear antibody was positive in all patients. Patients with dsDNA positivity had severe renal involvement.

Conclusion: Examination of skin for disease specific as well as nonspecific lesions is important in SLE as skin is one of the most important target organs. A good knowledge about the various cutaneous manifestations will help not only in diagnosis and management but also in predicting the prognosis.

Key words: Antinuclear antibody, Cutaneous manifestations, Disease activity, Systemic lupus erythematosus

INTRODUCTION

Lupus erythematosus is a systemic autoimmune disorder associated with polyclonal B cell activation that is thought to result from interplay of genetic, environmental, and hormonal elements. It is convenient to consider the heterogenous clinical expression of this disorder as constituting disease continuum or spectrum extending from a limited cutaneous disorder to a life-threatening systemic disease process.[1]

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Cutaneous lesions in patients with LE can be divided into two broad categories.

- LE specific skin lesions
- LE nonspecific skin lesions.

It is important to divide cutaneous lesions into LE specific and nonspecific because it is possible to make a diagnosis of LE from the histopathology of specific lesion only and not from nonspecific lesion. Nonspecific lesions are important in assessing the disease activity and are seen frequently in patients with systemic lupus erythematosus (SLE).[2] LE

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specific skin lesions are further subdivided into:

- Chronic cutaneous LE (discoid lupus erythematosus [DLE]) - localized DLE, generalized DLE, hypertrophic DLE, lupus panniculitis (lupus profundus)
- Subacute cutaneous LE (SCLE) - papulosquamous (psoriasiform) SCLE, annular polycyclic SCLE
- Acute cutaneous LE (SLE) - malar rash, wide spread erythema of sun exposed area, bullous, or toxic epidermal necrolysis (TEN) like acute cutaneous lupus erythematosus lesion.[2,3]

A variety of factors have been proposed to be etiologic for SLE[4] which include genetic factors, environmental factors, abnormalities in immune regulation, viral infection, drugs, and ultra violet rays.

Pathogenesis of SLE include abnormal production of auto antibodies and immune complexes, failure to suppress the production and proliferation of forbidden clones.[5] The American College of Rheumatology (ACR) criteria is used for diagnosis of SLE. Four main cutaneous manifestations are included in the ACR criteria which are malar rash, discoid rash, painless oral ulcer, and photosensitivity. Cutaneous lupus erythematosus disease area and severity index is used to assess the disease activity. It includes erythema, scaling, mucosal lesion, and nonscarring alopecia.[6] A better understanding of the various cutaneous manifestation of SLE is required for diagnosis, assessing the severity and prognosis, for choosing the optimum treatment option.

MATERIALS AND METHODS

A retrospective study of the various cutaneous manifestations in SLE was conducted in the Department of Dermatology, Madras Medical College and Rajiv Gandhi Government General Hospital. Data of SLE patients who attended skin department at our hospital from May 2015 to April 2016. History regarding nature of onset, progression, precipitating or exacerbating factors and symptomatology of skin lesion and systemic manifestation was taken. Patient's clinical examination details with reference to symptomatology, morphology, and distribution of skin lesion were also noted.

Biopsy was performed to confirm the diagnosis. Specific investigation including anti-nuclear antibody titer, anti-dsDNA estimation as well as nonspecific investigation such as total count, differential count, erythrocyte sedimentation rate (ESR), hemoglobin, red blood cells and platelet count, urine examination for albumin, sugar and deposits, renal function test, liver function test, electrocardiogram, X-ray chest, physical therapy (PT), activated partial thromboplastin time, bleeding and clotting time, Voluntary Counseling and Testing Centers, Venereal Diseases Research Laboratory was done. In addition, based on the symptoms clinical and laboratory abnormalities further tests were done if necessary including echocardiography, ultrasound abdomen, computed tomography brain, bone marrow aspiration, endoscopy, and renal biopsy.

RESULTS

Of 110 patients, maximum patients 52 among 110 were in the age group 21-30 years (47.2%). Male to female ratio was 1:9. Youngest patient was 9-year-old girl and eldest was 65-year-old female. The mean age of onset was 27 years (Table 1).

The probable precipitating or exacerbating factor was found in 79 of the total patients. The most common precipitating or exacerbating factor was found to be photosensitivity which was seen in 66 patients (60%). Infections such as typhoid, malaria, viral fever preceded the onset of SLE in 7 patients. One patient was diagnosed to have extra pulmonary tuberculosis and was started on anti tuberculous treatment. A total of 6 patients reported worsening of symptoms with mental stress. Two patients had exacerbation of disease during pregnancy. One patient had second trimester miscarriage due to exacerbation of disease and disease worsened further after abortion (Table 2).

Fever and fatiguability was present in 100% of cases. Malar rash was the most common specific skin lesion in 73 patients (66.36%). Discoid rash was seen in 20% of patients. Two patients had DLE lesion on scalp with

Table 1: Distribution of study patients in age group and gender

Age group	Female	Male	Total
0-10	1	-	1
11-20	7	1	8
21-30	46	6	52
31-40	37	4	41
41-50	3	-	3
51-60	4	-	4
61-71	1	-	1
	99	11	110

Table 2: Distribution of precipitating or exacerbating factor in study group

Precipitating/exacerbating factor	Number of patients
Photosensitivity	66
Infection	7
Mental stress	6
Pregnancy	2

scarring alopecia and depigmentation. Mucous membrane lesion was seen in 70% of patients, most commonly involving hard palate and buccal mucosa. Other mucosal lesions seen were gingivitis, glossitis, nasal ulceration, blepharitis, and conjunctivitis. Two patients had extensive erosions of oral cavity and erosion over labia majora.

Diffuse hair loss was mainly in the form of nonscarring alopecia in 88 patients (80%). Scarring alopecia was seen in only seven patients (6.36%). Bluish discoloration of finger nail and or toe nail was seen in 18 patients (16.36%). Among this, three patients had discoloration from the onset of disease. 2 patients were on chloroquine treatment for 3 months and showed bluish discoloration of all finger and toe nail and in one patient lunula was absent. Raynaud's phenomenon was present in 11 patients (10%). Other vascular lesions noticed were leg ulcers in 11 patients (10%), palpable purpura, peripheral gangrene, and erythema multiforme.

Systemic manifestations include musculoskeletal problems mainly arthralgia in 95 (86.36%), renal in 51 (46.36%),central nervous system including seizure, psychosis, hemiparesis, poor memory in 47 (42.72%), gastrointestinal and pulmonary complication in 15 (13.63%) patients each, eye involvement in the form of conjunctivitis, blepharitis, retinal hemorrhage, and lymphadenopathy were noted in 7 patients (6.36%) each. Menstrual irregularities were seen in 4 patients (3.63%).

Associated skin diseases were ichthyosis vulgaris in 11 patients (10%), chronic eczema in 8 patients (7.3%), superficial fungal infections including tinea cruris and pedis, pityriasis versicolor, oral candidiasis in 22 patients (20%), scabies in 7 patients (6.36%), and herpes zoster in 4 patients (3.63%) (Table 3).

Table 3: Distribution of disease specific and nonspecific lesion in study group

Lesions	Patients (%)
Disease specific lesions	
Malar rash	73 (66.36)
Discoid rash	22 (20)
Oral ulcer	77 (70)
Nonspecific lesion	
Alopecia	
Non scarring alopecia	88 (80)
Scarring alopecia	7 (6.36)
Nail change	18 (16.36)
Vascular	
Raynaud's phenomenon	11 (10)
Leg ulcer	11 (10)
Palpable purpura	7 (6.36)
Peripheral gangrene	4 (3.63)
Erythema multiforme	7 (6.36)

Laboratory abnormalities in 103 (93.63%) patients showed increased ESR, whereas 73(63.36%) patients had anemia. Thrombocytopenia was noted in 15 patients (13.63%). Deranged renal parameters were seen in 51 (46.36%) patients. All patients were positive for AntiNuclear Antibodies, 110 patients. Anti dsDNA was positive in 66 (60%) patients. Anti Cardiolipin antibodies and RF factor in 4 patients (3.63%). Renal biopsy with evidence of lupus nephritis was seen in 59 (53.63%).

Five patients had active disease flare up and succumbed to its complication. Three patients died due to end stage renal disease, one patient due to multiple cerebral infarctions and one patient due to TEN following anti tuberculous treatment.

DISCUSSION

SLE is a multiorgan autoimmune disease of unknown etiology with many clinical manifestations. The skin is one of the target organs most variably affected by the disease.[7]

Evidence for genetic factor involvement is due to occurrence of SLE in monozygotic twins and familial cases, studies from dermatoglyphics, increased the incidence of connective tissue disease, antinuclear antibody (ANA) positivity, hyperglobulinemia in patients relatives and HLA association particularly HLA B8,HLA DR 3.[7]

Sex hormones are known to influence SLE, an auto immune disease as estrogens enhance immuno enhancing, whereas androgens are immunosuppressive.[8] In this study, females predominated with female to male ratio of 9:1 comparable to study by Rowell *et al.*[9] and Malaviya, *et al.*[10] in which a female to male ratio was 8:1. Another study by Kole and Ghosh reported a ratio of 14:1.[11]

Peak age of onset was 27 years in this study. Higher mean age of onset was noted by Masi *et al.*[12] as 31 years and 3rd to 4th decade by Rowell[9] whereas 25 years by Kole and Ghosh[11] 24 years by Malaviya.[10] Even though SLE is considered a disease of young adults, the oldest age of onset was reported as 87 years by David *et al.*[9] In the present study group, the oldest age of onset was observed to be 65 years.

In this study, photosensitivity was present in 60% of patients and was the probable precipitating or exacerbating factor and the incidence was same as noted by Rowell *et al.*[11] LE specific skin lesion malar rash was seen in 66.36% comparable to study by Sontheimer[13] who quotes that the maximum occurrence of about 61%. Wysenbeek, *et al.*[14] reported malar rash in 49% and Vaidya, *et al.*[15] 53.18% of

the patients. Discoid rash was present in 20% of patients comparable to the observed the incidence of 20-50% by David *et al*.[8] The incidence of oral ulcer was 70% in this study which was very high when compared to 9.1% reported by Dubois[16] 64% by Malaviya[10] 56.67% by Kole and Ghosh.[11] Malar rash and oral ulcer had a parallel course with disease activity.

Hair loss was present as nonscarring alopecia in 86% and scarring alopecia in 6.3%, comparable to study by Kole and Ghosh[11] as 86.67% higher number than reported by Gilliam *et al*.[17] as 60% and 57% noted by Wysenbeek[14] of nonscarring hair loss. Bluish nail discoloration was seen in 16.36 % similar reports by kapadia.[18]

Among vascular lesions Raynauds phenomenon was the most common in 10% of patients similar to study by Kole and Ghosh[11] 6.67% of the cases, higher numbers were reported by Malaviya, *et al*.[10] 32% and Vaidya, *et al*.[15] 15.5%. Three patients had oral ulcer along with Raynauds phenomenon. The incidence of peripheral gangrene was observed to be 3.63% compared to higher reports of 9% by Moschella.[2] Leg ulcers were present in 10% of patients in accordance with reports of 5 to 29% by David *et al*.[8] 2 patients with leg ulcers had classical SLE manifestation along with reduced platelet count and hypocomplementemia [c3,c4] which may account for chronicity of leg ulcer. In one patient who had associated rheumatoid arthritis the leg ulcer was chronic and persistent probably due to overlap of SLE and rheumatoid arthritis. 7 patients had SLE with EMF overlap (Rowells) with typical target lesions and extensive oral ulceration almost similar to incidence quoted by David *et al*.[8] In one case of childhood SLE the disease had a florid course with extensive photosensitivity, lymphadenopathy, pneumonia and peri orbital puffiness. In addition to increased ESR and mild thrombocytopenia, ANA and anti ds DNA were positive. In spite of all bad prognostic factors patient remarkably improved with systemic steroids.

Elderly patients with SLE are characterized by a milder serological picture, infrequent renal disease and more Serositis and arthritis.[16] The oldest patient in our study group with 65 years had severe arthritis, easy fatiguability, fever,malar rash, nonscarring alopecia and contrary to reports had puffiness of face and evidence of renal involvement which is usually infrequent in elderly.

Among the hematological abnormalities, a raised ESR was found in 93.63%; even though, it may not be specific but helpful in assessing the severity of the disease. Anemia was detected in 63.36% of patients which was in accordance with reports of 50% by Dubios.[16] Anemias can result from chronic disease, auto immune hemolysis, iron deficiency, and chronic renal failure. Thrombocytopenia was present in 13.63% of patients correlating well with 14% incidence reported by Dubios.[16] One patient had decrease in PT and partial thromboplastin time. This patient had a history of spontaneous abortion along with flare up of SLE and decreased complement level. ANA was positive in all patients in this study. Nearly 60% of patients had positive antids DNA positivity and had severe renal involvement. One case of antiphospholipid syndrome in a female patient with 24 years had a family history of dermatomyositis in father supporting genetic factor in etiology of SLE.

Vasculitic skin lesions in some cases are associated with neuropsychiatric manifestations of lupus.[19] Such an association was not seen in the present study. Patients having bullous skin lesions had systemic flares that were reported by Malcangi *et al*.[20] An association between concomitant lupus nephritis and bullous lesions had been documented by Ng *et al*.[21]

CONCLUSION

Lupus erythematosus is a systemic disease with varied systemic as well as cutaneous manifestations. About 90% of patients have involvement of skin. Skin lesions can help in the diagnosis of SLE as well as to assess the severity, prognosis and also help in the management of SLE. Not only the specific lesion but nonspecific disease related skin lesions also play an important role in SLE as the disease severity is seen to go parallel with skin lesions. Better understanding of cutaneous lesions can help in providing better care to patients.

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Original Article

Evaluation of Peripheral Lung Masses with Special Reference to Ultrasound-guided Fine Needle Aspiration Cytology: A Clinico-radiological and Pathological Study

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Abstract

Introduction: New developments in the field of thoracic oncology are challenging the pathological diagnostic approach of lung cancer.

Objective: The aim of this study is to correlate the clinico-radiological findings with pathological findings of lung masses and to evaluate diagnostic value of ultrasound (USG)-guided transthoracic fine-needle aspiration cytology (FNAC) in peripheral lung masses.

Design: A prospective study carried out between September 2011 and August 2012 in the Department of Pulmonary Medicine, S. C. B. Medical College & Hospital, Cuttack, Odisha.

Methodology: A total of 40 patients with peripheral lesions adjacent to chest wall with accessibility through USG window were evaluated. FNAC were performed with lumbar puncture needle 20 G under USG guidance. Cytology results correlated with clinico-radiological findings and data analyzed.

Results: Definitive histological diagnosis made in 39 out of 40 patients (97.5%); 30 were malignant lesions and 9 benign. Among the malignant lesions, 13 were adenocarcinoma (33.3%), 9 were squamous cell carcinoma (23.1%), large cell carcinoma 1 (2.6%), anaplastic carcinoma 2 (5.5%), and small cell carcinoma (SCC) were 5 (12.8%). The benign lesion consisted of 7 inflammatory, 1 tubercular, and 1 fungal. In 1 patient diagnosis was inconclusive due to inadequate specimen.

Conclusions: USG-guided FNAC is safe, less expensive, less time consuming, less invasive diagnostic tool with high degree of accuracy and no radiation toxicity.

Key words: Cytology, Fine-needle aspiration cytology, Lung mass, Ultrasound

INTRODUCTION

New developments in the field of thoracic oncology are challenging the pathological diagnostic approach of lung cancer. Since specific therapies are now available for different histological tumor types diagnosis has to be specific and precise. After discovery of specific molecular alterations that are capable of predicting response to certain drugs, molecular testing of tumor cells is not considered a luxury, but rather necessary. The vast majority of lung cancer is diagnosed in advanced clinical stages, where cytologic or small biopsy material is the only form of tissue diagnosis, thus placing cytology, especially fine-needle aspiration cytology (FNAC) in the frontline for management of patients with lung cancer.[1] FNAC not only distinguishes benign from malignant lesions but also

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helps in tumor typing of lung cancer, thereby avoiding unnecessary delay in initiation of specific therapy such as chemotherapy or surgery.[2]

Aim and Objective

To study the correlation of clinico-radiological and pathological findings of peripheral lung masses and to determine the utility of ultrasound (USG)-guided FNAC in diagnostic evaluation of such lesions.

METHODOLOGY

The study was conducted in the Department of Pulmonary Medicine, S. C. B. Medical College, Cuttack in collaboration with the Department of Radiodiagnosis and Department of Pathology from September 2011 to September 2012. Patients with chest radiograph finding of mass lesion in peripheral lung fields were considered eligible for the study. The study participants were explained about their clinical diseases, procedure to be carried out and nature of the study in their own language and an informed consent was obtained. Exclusion criteria were mediastinal mass lesion, mass present more than 8 cm deep to skin surface and those who did not give their consent. After patients were enrolled into the study a detailed history was collected followed by thorough clinical examination. Routine blood investigations including coagulation profile and viral markers were performed. The subjects were kept nil per orally for 6 h before procedure. Only mild sedation was used for anxious patients. 22/23 gauze bore needles were used for fine-needle aspiration; 1.5 inch length needle for superficial masses and 8 cm long spinal needle for deep-seated lesions. Aspiration was performed under continuous real time USG visualization, that is, "guidance method" using "free hand approach." The needle was inserted through the skin directly into the plane of view of the transducer. This approach offers great flexibility to the operator by allowing subtle free hand adjustments to be made during the course of the FNAC, thereby compensating for improper trajectory and patient movement. After preparation of the site, 5 ml of 2% xylocaine was infiltrated into the skin, subcutaneous tissue, muscle plane, and parietal pleura. After the needle was visualized at the proper site the inner stylet was removed. A volume of 10 ml syringe was attached to the tail end of the needle. Several 1 cm up and down movements were made within the lesion. 1-2 passes were made most of the time. The suction was maintained for 30-45 s till some material appeared at the nozzle. When aspiration was completed, the negative pressure was slowly released before withdrawing the needle to equalize the pressure in the syringe. The needle was then withdrawn and pressure was applied at the puncture site for 3-5 min with sterile cotton to prevent hemorrhage or formation of hematoma. Gross evaluation of the aspirate was performed on-site by naked eye examination or by quick differential staining. If samples were inadequate repeat aspiration was done. The participants were kept under observation for 2-3 h. Chest radiographs were done before discharging the patient to rule out any complications of the procedure. For sterility the transducer was cleaned with isopropyl alcohol and placed directly on the skin. Sterile gel was used as an acoustic agent.

Clinico-radiological diagnosis made before FNAC procedure was correlated with cytology results and data were analyzed.

RESULTS

Total number of the study participants in the study were 40; 29 (72.5%) males and 11 (27.5%) females. Half of the subjects, that is, 20 belonged to age group of 45-64 (Table 1). The most common symptom was cough present in 92.5% followed by chest pain in 52.5% of patients. Clubbing was found in 20 (50%), pallor in 21 (52.5%) and superior vena caval syndrome seen in 6 (10%) (Table 2). Nearly 75.9% of male patients (22) were smokers, whereas none of the female patients had smoking history (Table 3). Smoking index of smokers were <300 in 16, 300-600 in 4 and >600

Table 1: Age and sex distribution of cases with lung mass

Age group (in years)	Number of cases (%)	Male (%)	Female (%)
25-34	6 (15)	4 (10)	2 (5)
35-44	3 (7.5)	0 (0)	3 (7.5)
45-54	12 (30)	8 (20)	4 (10)
55-64	8 (20)	6 (15)	2 (5)
≥65	11 (27.5)	11 (27.5)	0 (0)
Total	40 (100)	29 (72.5)	11 (27.5)

Male: female=2.64:1, maximum numbers of patients belong to age group 45-54 years (12 cases), minimum numbers of patients belong to age group 35-44 years (3 cases)

Table 2: Symptoms and signs in patients of lung mass

Clinical symptoms and signs	Number of cases (%)
Cough	37 (92.5)
Hemoptysis	11 (27.5)
Chest pain	21 (52.5)
Breathlessness	14 (35)
Constitutional symptoms	31 (77.5)
Clubbing	20 (50)
Lymphadenopathy	7 (17.5)
Pleural effusion	4 (10)
Pallor	21 (52.5)
Superior venacaval syndrome	6 (10)

Distribution of symptoms and signs in patients of lung masses. Most common symptoms were cough and constitutional symptoms. Most common signs were pallor followed by clubbing

in 2 (Table 4). Of 40 FNAC procedures done 39 samples were adequate, that is, 97.5% and only 1 sample was inadequate where diagnosis could not be made. Malignancy was detected in 30 patients (75%) and 9 cases (22.5%) were non-malignant (Table 5). In non-neoplastic samples, 1 was tubercular, 1 fungal, and 7 were inflammatory. Most common type of lung cancer was adenocarcinoma (43.3%) followed by squamous cell carcinoma (30%) and SCC (16.67%) (Table 6). Of 39 patients where USG-guided FNAC could reach a diagnosis clinico-radiological and pathological correlation were seen in 35 cases, that is, 89.74% (Table 6). Complications due to the procedure were observed in 8 patients; 5 patients complained of chest pain whereas vasovagal pain, hemoptysis, and pneumothorax occurred in 1 patient each. Patient with pneumothorax was managed with intercostal chest tube drainage and was discharged in 3 days after complete lung expansion while other patients were managed conservatively.

Table 3: Smoking status in lung mass

Sex	Number of patients	Smoker number (%)	Non-smoker number (%)
Male	29	22 (75.9)	7 (24.1)
Female	11	0 (0)	11 (100)

Association with smoking habit shows among the 29 males, 22 were smokers (75.9%) and 7 were non-smoker (24.1%). None of the females were smokers

Table 4: Smoking index

Smoking index	Number of patients (%)
0	18 (45)
1-300	16 (40)
301-600	4 (10)
>600	2 (5)

Out of 22 smokers, 16 cases (40%) had smoking index in between 1 and 300, 4 cases (10%) had smoking index 301-600 and 2 cases (20%) had smoking index>600

DISCUSSION

FNAC was first used by Martin and Ellis as a diagnostic tool.[3] Leyden in 1833 and Manbriel in 1986 introduced the technique as diagnostic lung puncture for the detection of malignancy and infections.[4] In the last decades, FNAC of pulmonary mass has gained popularity as an useful test for cytological analysis of lung and mediastinal pathologies. It has been used successfully as a nonsurgical tool for confirmation of primary as well as metastatic lesions.[5]

The present study constituted 29 males (72.5%) and 11 females (27.5%) out of the total 40 with a male:female ratio of 2.64:1 (Table 1). The age ranged from 26 to 82 years. Although many studies have reported high male: female ratio, attributing it to more exposure to toxic substance and outdoor life of males, some recent documentation shows fall in incidence in males and increases in females.[6] This study has similar findings as Tan *et al.*, with male:female ratio of 2.53:1 with age ranging from 11 to 82 years.[7] Most common age group for malignancy in this study is >65 years (23.7%). Tan *et al.,* also found malignant lung tumor most common in people with age of >50 years and more.[7] Detection of 38.5% of malignancy in <50 years age in this study is close to the finding of

Table 5: Pathological diagnosis of lung mass

Total number of cases	FNAC		Pathological diagnosis	Male	Female	Total	Inadequate material/inconclusive cases
	Not done	Done					
			Adenocarcinoma	10	3	13	1 case
			Squamous cell carcinoma	7	2	9	
			SCC	2	3	5	
			Large cell carcinoma	1	0	1	
			Anaplastic carcinoma	2	0	2	
			Fungal	1	0	1	
			Tubercular	1	0	1	
			Inflammatory	6	1	7	
40	-	40		30	9	39	1

Results of FNAC: Most common pathological diagnosis was adenocarcinoma lung. FNAC: Fine needle aspiration cytology, SCC: Small cell carcinoma

Table 6: Correlation of clinico-radiological versus pathological diagnosis

Type of lesion	Clinico-radiological diagnosis	Pathological diagnosis			Micro biology
		Correct	Incorrect	Inconclusive/inadequate material	
Lung mass (n=40)					
Malignant	30	28	2	-	-
Tubercular	1	1	-	-	Positive
Inflammatory	8	5	2	1	-
Fungal	-	1	-	-	Positive

Clinico-radiological and pathological correlation of lung mass in the present study is 35/39 (89.74%)

Behera and Balamugesh who reviewed data from national research registry program of ICMR and found that 40% of lung cancer occurred in <50 years of age.[8]

The risk of malignancy increases in smoking index. It is the product of average number of cigarettes per day and total period of smoking in years. In the study of Rajsesekharan *et al.*, 73.2% of patients were smokers and 66.4% of smokers had smoking index above 300.[9] Number of smokers for Guleria *et al.,* were 58% and for Jindal and Behera were 83.5%.[10,11] In this study, 22 out of 40 male patients (75.9%) were smokers. None of the female patients were smokers (Table 3). 6 patients (27.3%) had smoking index >300 (Table 4).

In the present study of adequacy of sampling was 97.5%. Adequacy of sample in more than 90% of cases was also reported in previous studies, that is, Clee *et al.*, Hollings and Shaw, Behera and Balamugesh.[8,12,13] The cytology specimen evaluated in our study (Table 5) showed definite malignancy in 75%, inflammatory lesions in 17.5%, tuberculosis in 2.5%, and fungal in 2.5%. Similar observations were made by Bandyopadhyay *et al.*, with malignant lesions in 67.4%, benign and inflammatory lesions in 19.5%, atypical cells in 5.8% and granulomas in 7.8%.[14] Tan *et al.*, also observed 65.8% malignant lesions, 25.4% inflammatory/nonmalignant lesions and TB in 5.3%, with an yield of 93%.[7] Dahlstrom *et al.*, Gouliamos *et al.,* reported 64.6% and 61% malignant lesions, respectively.[15,16] A higher value was reported by Ahmad *et al.,* with malignancy in 78% of cases and TB in 12% of cases.[5] Distinction of nonsmall cell lung carcinoma (NSCLC) from SCC was important as most of the therapeutic decision needed this degree of differentiation and it was highlighted by previous studies.[7,17,18] Pathak *et al.,* observed NSCLC in 75-80% of malignant lesions with increasing the incidence of adenocarcinoma which is similar to this study.[19] An update on non SCCs attributed this increasing incidence of adenocarcinomas to use of filter cigarettes which are of low tar and tend to be inhaled deeply resulting in carcinogen to be deposited more peripherally. Tan *et al.,* also reported a high incidence of adenocarcinomas in 49.4% of cases, where the most of lesion were peripheral in distribution.[7] They reported squamous cell carcinoma in 12%, SCC in 9.4% and metastatic lesion in 8% of cases.

Needles of 22-23 G were used for most aspirates in the present study with a reproducibility percentage of 97.5%. The Papanicolaou Society of Cytopathology Task Force (1999) also opined the use of 22 G Chiba or Grenne needle. It was found that by using 25 G needle for emphysematous lung, COPD and coagulopathy, the sample was adequate in 88.5%,[20] also pneumothorax was avoided by use of thinner needle.[21] The complication recorded in the present study was only in 8 cases. Chest pain was the most common complication observed in 5 (12.5%). Pneumothorax was observed in 1 case (2.5%), vasovagal reaction in 1 case (2.5%), and hemoptysis in 1 cases (2.5%) which were mild enough to be managed conservatively. Near similar complication rate was noted by few earlier studies.[14,22]

The clinico-radiological diagnosis was compared with the pathological diagnosis in 39 cases. In 35 cases, the clinico-radiological diagnosis was well correlated with the pathological diagnosis. Clinico-radiological suspicion was proven wrong pathologically in 4 cases; 1 suspected lung malignancy reported fungal, another suspected lung malignancy reported benign, and 2 suspected benign lesions were malignant. Diagnosis was inconclusive in 1 case due to inadequate specimen. The clinico-radiological and pathological correlation of Thoracic mass in this study is 89.74% which is statistically significant ($P = 0.0001$) with a sensitivity of 93.33% and specificity of 77.77% (Table 6). Torkian *et al.,* observed that of all radiologically indeterminate solitary pulmonary nodules, 50% were malignant and of all the lesion <5% lung neoplasm were benign. So when a clinician suspects neoplasia, then there is a high probability that the lesion is malignant.[23]

CONCLUSION

Although thoracotomy and biopsy is the most accurate method of diagnosis, USG-guided FNAC is a safe, less expensive, less time-consuming, less invasive diagnostic tool with high rate of accuracy. Such procedure can be adopted safely by the physicians and the coordination of pulmonologist, radiologist and pathologist is highly essential for better yield.

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Original Article

Effectiveness of Posterior Mitral Leaflet Preservation in Mitral Valve Replacement Surgery: A Prospective Study

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Abstract

Introduction: Mitral valve replacement with chordal preservation requires technical skill, long cross clamp time and prolonged ischemic time of myocardium.

Materials and Methods: All patients undergoing mitral valve replacement in the Department of Cardiothoracic Surgery, Government Rajaji Hospital during December 2009 to December 2011 were included in the study.

Results: All the observations are depicted in tabular form.

Conclusion: In this study, the partial preservation of chordae was compared with classical mitral valve replacement. Since the partial chordal preservation (posterior mitral leaflet preservation) is simpler it can be performed in all centers with effective advantages of implanting an ideal valve without compromising the size and function of the prosthetic valve.

Key words: Mitral valve, PML preservation, Post-operative left ventricular function

INTRODUCTION

Mitral valve replacement with chordal preservation requires technical skill, long cross clamp time and prolonged ischemic time of myocardium. At the same time, chordal preservation improves the post-operative left ventricular function and exercise induced ejection fraction of the patient. However, in the mitral stenosis, it can lead to implantation of smaller valve.[1-5]

To study the effectiveness of posterior mitral leaflet (PML) preservation during mitral valve replacement on post-operative left ventricular functional improvement compared to the classical mitral valve replacement.

The parameters analyzed were left ventricular ejection fraction, left ventricular end systolic and diastolic dimension, left ventricular mass pre and postoperatively, immediate hemodynamic stability and long-term left ventricular function during exercise. These parameters were analyzed preoperatively and at the end of 6 months postoperatively.

The PML preservation in mitral valve replacement was compared with classical mitral valve replacement both techniques have their own advantage and disadvantages.

In classical mitral valve replacement, all the papillary muscular chordae were removed to facilitate bigger size valve implantation, shorter cross clamp time, technical simplicity, and less ischemic time for myocardium.

In our study, we comparing this two techniques by pre- and post-operative analysis of left ventricular function with the help of echocardiogram (ECHO) and NYHA class symptom of the patients preoperatively and 6 months post-surgery.

The study was conducted as a nonrandomized control trail. The procedures were decided preoperatively after examining the mitral valve anatomy.

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MATERIALS AND METHODS

All patients undergoing mitral valve replacement in the Department of Cardiothoracic Surgery, Government Rajaji Hospital during December 2009 to December 2011 were included in the study.

Patients having rheumatic mitral stenosis, rheumatic mitral valve replacement. All the patients were implanted TTK chitra valve varying from size 23 to 27 mm.

The pre- and post-operative ECHO evaluation was done in the Cardiology Department in Government Rajaji Hospital.

The post-operative follow-up ECHO was done at 10th post-operative day was done followed by ECHO evaluation at the end of 6th month. During ECHO evaluation left ventricular ejection fraction (LVEF), left ventricular diameter in diastole, left ventricular diameter in systole, left ventricular end systolic volume, left ventricular end diastolic volume, left ventricular mass index and exercised ejection fraction at 6th month were evaluated and analyzed.

A total of 40 patients underwent valve replacement from 2009 to 2011. Out of 40 patients, 25 patients had mitral valve replacement with PML preservation. 15 patients underwent mitral valve replacement with anterior mitral leaflet and PML resection.

Pre- and post-operative function NYHA class and ECHO evaluation were compared and analyzed.

RESULTS

Most of the cases were in 35-46 age group, very few patients were older than 45 years (7.5%) (Table 1 and Figure 1).

In Table 2, PML preserved group there were 11 males and 14 females, in the PML resected group, there were 8 males and 7 females.

In PML preserved group, 50% of patients had TTK valve implanted with size 25 or less. In the PML resected group, 60% of patient had bigger size valve implanted. This shows that PML resected group has a possibility of bigger size prosthetic valve implantation (Table 3 and Figure 2).

Ventilatory support for both group of patients extended from a minimum of 18 h to maximum of 48 h there was no significant advantage of PML preservation on the duration of ventilation (Table 4).

Tables 5 and 6 show that post-operative NYHA class of PML preserved group shows marked improvement. At that same time, PML resected groups were in higher NYHA class.

Table 7 shows the post-operative LVEF of PML preserved groups had improved values. PML resected group showed no improvement in LVEF (ECHO evaluation done by Simpson method).

Table 8 shows post-operative left ventricular diastolic diameter of PML preserved group shows reduction in size compared to PML resected group. *P* value is

Table 1: Age distribution

Age in years	Male	Female	Total
16-25	3	4	7
26-35	5	7	12
36-45	9	9	18
>45	2	1	3
Total	19	21	40

Table 2: Sex distribution

Sex	PML preserved	PML resected	Number of cases (%)
Male	11	8	19 (47.5)
Female	14	7	21 (52.5)
Total	25	15	40 (100)

PML: Posterior mitral leaflet

Table 3: Size of valve

Size of valve in mm	PML preserved	PML resected	Total
TTK 23	3	3	6
TTK 25	12	3	15
TTK 27	9	5	14
TTK 29	1	4	5
Total	25	15	40

Chi-square *P*=0.679 not significant. PML: Posterior mitral leaflet

Table 4: Ventilation time

Ventilation time (in h)	PML preserved	PML resected	Total
18	10	0	10
24	11	12	23
36	1	1	2
48	3	5	5
Total	25	15	40

Chi-square *P*=0.886 not significant. PML: Posterior mitral leaflet

Table 5: PML preserved

NYHA class	Number of patients			
	I	II	III	IV
Pre-operative	0	0	25	0
Post-operative	23	2	0	0

Chi-square *P*=0.019 (significant). PML: Posterior mitral leaflet

significant (ECHO evaluation done by Simpson method) (Figure 3).

Table 9 shows post-operative left ventricular systolic diameter of PML preserved group shows reduced in size comparatively to PML resected group. *P* valve is significant (ECHO evaluation done by Simpson method).

In Table 10, post-operative left ventricular systolic volume of PML preserved group shows reduction in volume compared to PML resected group. *P* value is significant (ECHO evaluation done by Simpson method).

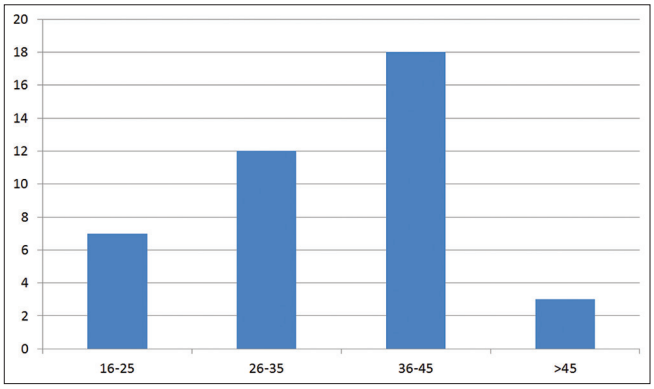

Figure 1: Post-operative ejection fraction

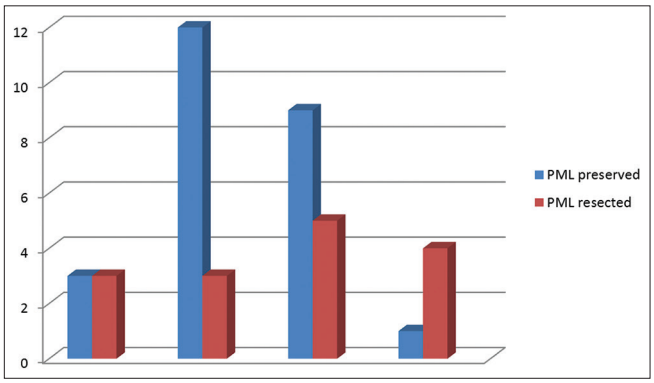

Figure 2: Post-operative left ventricular diameter in diastole

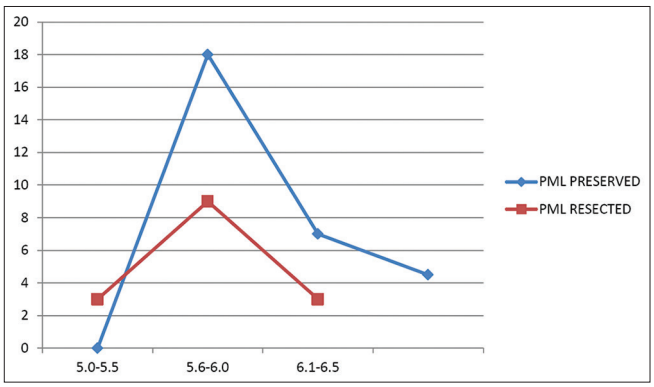

Figure 3: Post-operative left ventricular diameter in systole

In Table 11, post-operative left ventricular diastolic volume of PML preserved group shows reduction in volume compared to PML resected group. *P* value is significant (ECHO evaluation done by Simpson method).

Table 12 shows there was no significant advantage in heavy mass index reduction in the PML preserved compared to PML resected group (ECHO evaluation done by Simpson method).

Table 13 shows that at 6 months post-operative period, exercise ejection fraction was improved in PML resected

Table 6: PML resected

NYHA class	Number of patients			
	I	II	III	IV
Pre-operative	0	0	15	0
Post-operative	2	13	0	0

Chi-square *P*=0.003 (significant). PML: Posterior mitral leaflet

Table 7: LVEF

LVEF %	PML preserved		PML resected	
	Pre	Post	Pre	Post
45-50	8	2	14	15
51-55	12	12	1	0
56-60	3	10	0	0
61-65	2	1	0	0
Total	25	25	15	15

Chi-square *P*=0.048 significant. LVEF: Left ventricular ejection fraction, PML: Posterior mitral leaflet

Table 8: LVIDd

LVIDd in cm	PML preserved		PML resected	
	Pre	Post	Pre	Post
5.0-5.5	0	15	3	2
5.6-6.0	18	10	9	10
6.1-6.5	7	0	3	1
Total	25	25	15	13 (death-2)
Mean		6.008		5.556
SD		0.220		0.227
P	<0.001 significant			

LVIDd: Left ventricular dimension in diastole, SD: Standard deviation, PML: Posterior mitral leaflet

Table 9: LVIDs

LVIDs in cm	PML preserved		PML resected	
	Pre	Post	Pre	Post
2.8-3.4	0	4	3	2
3.5-3.8	17	21	8	5
>3.9	8	0	4	6
Total	25	25	15	13 (death-2)
Mean		3.852		3.484
SD		0.161		0.155
P value	<0.001 significant			

LVIDs: Left ventricular dimension in systole, SD: Standard deviation, PML: Posterior mitral leaflet

Table 10: LVESV

LVESV in ml	PML preserved		PML resected	
	Pre	Post	Pre	Post
25-35	0	10	4	2
36-45	4	15	3	10
46-55	17	0	8	1
56-65	4	0	0	0
Total	25	25	15	13 (death-2)
Mean		51.4		38.28
SD		5.66		3.95
P value	<0.001 significant			

LESV: Left ventricular end systolic volume, SD: Standard deviation, PML: Posterior mitral leaflet

Table 11: LVEDV

LVEDV in ml	PML Preserved		PML resected	
	Pre	Post	Pre	Post
<130	0	25	4	6
130-140	11	0	10	5
141-150	11	0	1	2
151-160	3	0	0	0
Total	25	25	15	13 (death-2)
Mean		144.28		113.4
SD		7.87		4.58
P value	<0.001 significant			

LVEDV: Left ventricular end diastolic volume, PML: Posterior mitral leaflet

group. *P* value is significant (ECHO evaluation by Simpson method by 6 min walk test) (Figure 4).

DISCUSSION

Mitral valve replacement surgery is the most common open heart surgery performed in the Department of Cardiothoracic, Government Rajaji Hospital, Madurai. Rheumatic mitral valvular disease is more common than degenerative mitral valve disease. Mitral valve repair is not possible in large number of patients because of rheumatic cicatrized subvalvular mitral valve disease. The prosthetic mitral valve replacement is commonly performed in our center. Because of economical reasons bioprosthetic valve were not implanted.

Mitral valve replacement is done either by preservation of all chordate to the mitral leaflet or by resection of both anterior and PMLs. There are many techniques of preserving chordate during surgery. PML and their chordates were commonly preserved in our center. The effectiveness of PML chordal preservation was analyzed and compared with classical mitral valve replacement. The study includes total of 40 patients; 25 patients were PML preservation and 15 patients had both anterior and PML resected.[5-8]

The procedure of choice was decided while doing surgery after examining the mitral valve. The study group included

Table 12: LVMI

LVMI	PML preserved		PML resected	
	Pre	Post	Pre	Post
150-160	7	11	6	4
161-170	18	14	8	8
>170	0	0	1	1
Total	25	25	15	13 (death-2)
Mean		159.56		161.28
SD		31.5		5.08
P value	0.789 not significant			

LVMI: Left ventricular mass index, PML: Posterior mitral leaflet, SD: Standard deviation

Table 13: LVEF %

Exercise LVEF %	Post-operative	
	PML preserved	PML resected
40-49	0	13
50-59	2	0
60-65	23	0
Total	25	13 (death-2)

LVEF: Left ventricular exercise ejection fraction, PML: Posterior mitral leaflet

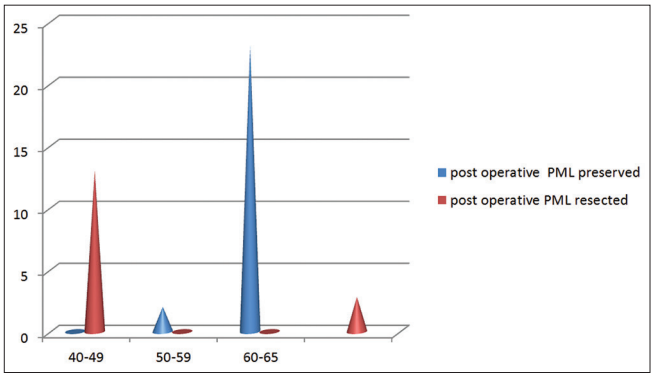

Figure 4: Post-operative ejection fraction with exercise

11 males and 14 female in PML preserved group; 8 males and 7 females in PML resected group.

In PML preserved group, the size of valve implanted was 25 and/or smaller than 25 size. At the same time, PML resection groups 60% if the cases had more than 25 size of prosthetic valve implanted. In PML resected groups had larger size valves implanted.

Out of the 40 cases, isolated mitral stenosis was 3 cases, mitral restenosis were 2 cases, and pure mitral regurgitation included 10 cases. All of them were of rheumatic etiology. The rest of the cases were of mitral stenosis with mitral regurgitation. The mitral and restenosis had mostly PML resection, because of severe subvalvular disease and for implanting the valve without hinderence of prosthetic valve movement. The statistical analysis of ventilatory support following surgery for the both groups was similar.

The complication in the PML preserved group was cerebrovascular accident in one case and heart block in 2 cases, 2 death occurred in PML resected group due to low output cardiac failure. The immediate post-operative ECHO study done on 10th day by Simpson method showed improvement in left ventricular ejection fraction in PML preserved groups, but there was no significant improvement in PML resected group.

After 6 months, patients in PML preserved group remain in NYHA Class I, but in PML resected group most of them were in NYHA Class II with significant effort in tolerance as shown by exercised left ventricular ejection fraction.

Statistical analysis of ECHO evaluation at 6 months showed marked improvement of post-operative left ventricular diastolic and systolic dimension, end diastolic and end systolic volume in PML preserved group. The *P* value is significant ($P < 0.001$). However, in the PML resected groups these parameters did not show any improvement.[9-12]

Hence, PML preservation is advantageous and a simpler procedure which can help the mitral valve replacement patients in long run when compared to PML resection.

Mitral valvular chordal preservation is done in many ways, total chordal and partial chordal preservation. In this study, partial preservation of chordate was compared with classical mitral valve replacement. Since partial chordal preservation (PML preservation) is a simpler technique, it can be performed in all centers with the effective advantage of implanting an ideal valve without compromising the size and function of the prosthetic valve. PMLs preservation contributes to post-operative improvement of patient symptoms and cardiac output index.[13,14]

CONCLUSION

In this study, the partial preservation of chordae was compared with classical mitral valve replacement. Since the partial chordal preservation (PML preservation) is simpler it can be performed in all centers with effective advantages of implanting an ideal valve without compromising the size and function of the prosthetic valve. PMLs preservation contributes to post-operative improvement of patient symptoms and cardiac output index.

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Original Article

Incidence and Predisposing Factors of Birth Trauma in a Tertiary Care Hospital in Chennai, India: A Prospective Study

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Abstract

Background: Birth trauma, especially mechanical trauma is one of the important causes of significant neonatal morbidity and rare cause of mortality. With advancement in technology and improved obstetric care and liberal use of cesarean section deliveries, serious birth trauma is decreasing worldwide.

Aim: The aim is to determine the incidence and predisposing factors of birth trauma in a tertiary care hospital.

Materials and Methods: This was a prospective, case-control study carried out at Government RSRM Hospital, Government Stanley Medical College, Chennai between October 2007 and September 2008.

Results: Head and neck injuries were the most common with 253 (88%) injuries, followed by skin and soft tissue injuries 17 (6%), nerve injuries 14 (5%), and bone injuries 4 (1%). No intra abdominal injury has been recorded. In our study, the predisposing factors for mechanical birth trauma were primiparity ($P < 0.0001$), short maternal stature ($P < 0.0001$), unbooked mother ($P = 0.0007$), antenatal obstetrical complications such as malpresentation ($P = 0.001$), cephalo pelvic disproportion ($P < 0.0001$), oligohydramnios ($P = 0.03$), late referrals from peripheral health institutions ($P < 0.0001$), breech presentation ($P = 0.001$), oxytocin use ($P < 0.0001$), obstructed labor ($P < 0.0001$), shoulder dystocia ($P < 0.0001$), instrumental delivery ($P < 0.0001$), size of the baby ($P < 0.0001$), birth weight more than 3.5 kg ($P < 0.0001$).

Conclusion: The incidence of serious birth injuries is very low but minor injuries are significantly high. Primiparity, obstructed labor, instrumental delivery, large baby, malpresentation are the risk factors identified in this study.

Key words: Instrumental delivery, Malpresentation, Mechanical birth trauma, Predisposing factors

INTRODUCTION

Labor is an intensive care situation. The woman and her unborn infant are at potential risk from unpredictable acute emergencies. In the context of increasing level of expectation, knowledge, and medico legal problems, it is the right of every prospective parent to be blessed with normal newborn. However, there are clinical situations inherent to that particular pregnancy when birth injuries are expected. These inherent factors could be maternal, fetal, type of assisted deliveries and finally the experience of the health worker conducting the delivery.

The 19th century was witness to many detailed autopsy clinical studies relating birth trauma to fetal presentation and mode of delivery. Despite a declining incidence due to improvements in obstetrical care and prenatal diagnosis, birth injuries remain a significant cause of morbidity and mortality.

The significance of birth injuries may be assessed by review of mortality data. In 1981, birth injuries ranked 6th among major causes of neonatal death, resulting in 23.8 deaths per 100,000 live births.[1] During ensuing decade because

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of refinements in obstetric techniques and the increased use of cesarean deliveries over difficult deliveries dramatic decline occurred in birth injuries as a cause of neonatal death. Statistics for 1993 revealed a reduction to 3.7 deaths per 100,000 live births.[2] The most recent figures available for 2005, the mortality rate in USA were 0.6/100,000 live births.[3]

The overall incidence of birth trauma reported from USA ranges from 6 to 8 injuries per 1000 live births (Perlow *et al.*, 1996).[4] The diagnosis and its notification in Indian setup is nearly impossible as the majority of deliveries are still conducted by unskilled, self-acclaimed birth attendants and even in tertiary medical institutions, autopsies are seldom performed. The Indian literature is deplete with information on birth trauma. Guha *et al.*, 1970, observed the incidence of birth trauma as 6.8/1000 live births.[5]

Injuries to the infant that result from mechanical forces (i.e., compression, traction) during the birth process are categorized as mechanical birth trauma.[6] Factors responsible for mechanical injury may coexist with hypoxic-ischemic insult; one may predispose the infant to the other. Nearly one half are potentially avoidable with recognition and anticipation of obstetric risk factors. Infant outcome is the product of multiple factors.

Many injuries such as soft tissue trauma are minor and self limiting but others such as liver lacerations, subgaleal hemorrhage or large subdural hemorrhage can be life-threatening and require prompt recognition and intervention. Mechanical Birth trauma can result in both physical and neuro developmental handicap.

Aim

To study the incidence of birth trauma and to analyze the factors predisposing to birth trauma.

MATERIALS AND METHODS

Case-control study was conducted in the Department of Neonatology in Government Stanley Medical College. All babies with Mechanical Birth Trauma delivered in RSRM hospital during the study were included in the study. Exclusion criteria: Still births, anoxic birth trauma, and caput succedaneum were excluded from the study. Babies born during the study were examined for mechanical birth trauma. If birth trauma present have been included as cases in this study. Detailed antenatal history and intra partum history, complete physical examination and relevant investigations done for obtaining diagnosis. The first normal baby born during the study period was taken as control and their antenatal and intrapartum history were obtained. Incidence, morbidity pattern and mode of treatment were given in frequencies and their percentage. Maternal weight, parity, weight, height, oxytocin use, duration of labor, shoulder dystocia, mode of delivery, neonatal variables such as sex, maturity, size of the, birth weight, and resuscitation requirements were analyzed using Pearson Chi-square test and Yates corrected Chi-square test.

RESULTS

The study group consists of 12735 babies. Out of them, 283 babies having 288 birth injuries were found as per inclusion criteria. 5 neonates had more than one injury. The incidence of birth trauma was 22.22/1000 live births.

Head and neck injuries were the most common with 253 (88%) injuries, followed by skin and soft tissue injuries 17 (6%), nerve injuries 14 (5%), and bone injuries 4 (1%). No intra abdominal injury has been recorded (Table 1).

Considering the individual injuries subconjunctival hemorrhage recorded in 107 (37%) babies with an incidence of 0.84% of live births. Cephalhematoma was found in 72 (25%) babies, an incidence of 0.57%. In head and neck injuries, abrasions, ecchymoses, laceration found in 31 (10.8%), 23 (7.9%), 8 (2.8%) babies an incidence of 0.24%, 0.18%, and 0.06%, respectively. Soft tissue contusion and laceration recorded in 13 (4.51%), and 4 (1.39%), respectively, an incidence of 0.13% when combined together. Subgaleal Hemorrhage found in 6 (2.08%) neonates an incidence of 0.47/1000 live births. Auricle injury noted in 5 (1.74%), an incidence of 0.4/1000 live births. Sternomastoid tumor was found in 1 (0.35%) baby, an incidence of 0.08/1000 live births. Brachial palsy was found in 10 (3.47%), an incidence of 0.8/1000 live births. Out of this total brachial palsy found in 3 (30%) cases. Facial nerve palsy was found in 4 (1.39%) neonates an incidence of 0.31/1000 live births. In bony injuries Fracture clavicle, femur, and humerus was recorded in 1 (0.35%), 2 (0.7%), and 1 (0.35%) babies, respectively an incidence of 0.08, 0.16, and 0.08, respectively.

An increased rate of primiparity was present which is statistically significant ($P < 0.0001$) (Table 2).

Maternal short stature found in study group was 41 (14%) compared to 4 (1%) in control group which is statistically significant ($P < 0.0001$, odds ratio: 15, confidence interval [CI] [5-51]).

13 (5%) mothers were unbooked in the study group compared to 2 (0.5%) in control group ($P = 0.0007$, odds ratio: 9, CI [2-56]).

Table 1: Incidence of birth trauma based on types

Type of birth trauma	Cases *n*=283 (%)	Incidence percentage *n*=12735 (%)	Incidence per 1000 live births
Head and neck injuries	248 (88)	1.95	19.5
Skin and soft tissue injuries	17 (6)	0.13	1.3
Nerve injuries	14 (5)	0.11	1.1
Bone injuries	4 (1)	0.03	0.3
Intraabdominal injuries	0	0	0
Total		2.22	22.2

Table 2: Distribution of parity in birth trauma

Parity	Cases *n*=283 (%)	Controls *n*=366 (%)	*P*-value
0	218 (77.03)	173 (47.27)	*P*<0.0001
1	55 (19.43)	158 (43.17)	
2	9 (3.18)	31 (8.47)	
>3	1 (0.35)	4 (1.1)	

Most common obstetrical complications found in study group are cephalo pelvic disproportion (CPD)/contracted pelvis 48 (16.96%), malpresentation 22 (7.77%), pregnancy-induced hypertension/pre-eclamptic toxaemia (PIH/PET)/eclampsia 12 (4.24%), gestational diabetes mellitus (GDM) in 8 (2.83%), multiple gestation and oligohydramnios 5 (1.77%) each. In control group PIH/PET/eclampsia 20 (5.46%), CPD 18 (4.92%), malpresentation 9 (2.46%), multiple gestation and GDM 3 (0.82%), nil oligohydramnios were found in decreasing order of frequency. Statistically significant increased rate of malpresentation ($P = 0.001$), CPD/contracted pelvis ($P < 0.0001$), oligohydramnios ($P = 0.03$) were found.

66 (23%) mothers in study group referred late from the peripheral health institutions (PHI) compared to just 6 (1.6%) in control group which is statistically significant ($P < 0.0001$).

Increased incidence of malpresentation found in study group (breech 23 [8.13%] and face 3 [1.06%]) compared to the control group (breech 9 [2.46%] and nil face presentation) which is statistically significant ($P < 0.0001$).The use of oxytocin was 181 (63.96%) in study group, compared to the control group 35 (9.56%) which is statistically significant ($P < 0.0001$, odds ratio: 16, CI [11-26]). The duration of labor was normal in 209 (73.85%), 365 (99.73%) in study and control group, respectively. Obstructed labor was seen in 74 (26.15%) in the study group compared to just 1 (0.27%) in control group, statistically significant ($P < 0.0001$, odds ratio: 124, CI [19-250]). Precipitate labor was not found in both study and control group. Shoulder dystocia was present in 19 (6.71%) deliveries in the study group compared to nil in control group ($P < 0.0001$) (Table 3).

Table 3: Perinatal factors in birth trauma

Perinatal factors	Cases (%)	Controls (%)	*P*-value
Presentation			
Vertex	257 (90.81)	357 (97.54)	0.0002
Breech	23 (8.13)	9 (2.46)	0.001
Face	3 (1.06)	0	0.05
Brow	0	0	n/a
Oxytocin use			
Yes	181 (63.96)	35 (9.56)	<0.0001
No	102 (36.04)	331 (90.44)	
Duration of labor			
Normal	209 (73.85)	365 (99.73)	<0.0001
Obstruted labor	74 (26.15)	1 (0.27)	
Precipitate labor	0	0	
Shoulder dystocia			
Yes	19 (6.71)	0	<0.0001
No	264 (93.64)	366 (100)	

Statistically increased rate of instrumentation was seen in the study group ($P < 0.0001$) (Table 4).

In babies with birth trauma 245 (86.57%) were characterized as appropriate for gestational age (AGA); 23 (8.13%) as large for gestational age (LGA); 15 (5.3%) as small for gestational age (SGA). In the control group, the size of the baby was AGA 308 (84.15%), SGA 57 (15.57%) and LGA 1 (0.28%). LGA babies were significantly increased in the study population ($P < 0.0001$).

The birth injuries were common in babies with a birth weight more than 3.5 kg. Birth weight distribution between groups was significant ($P < 0.0001$) (Table 5).

In our study, the predisposing factors for mechanical birth trauma were primiparity ($P < 0.0001$), short maternal stature ($P < 0.0001$), unbooked mother ($P = 0.0007$), antenatal obstetrical complications such as malpresentation ($P = 0.001$), CPD ($P < 0.0001$), oligohydramnios ($P = 0.03$), late referrals from PHI ($P < 0.0001$), breech presentation ($P < 0.0001$), oxytocin use ($P < 0.0001$), obstructed labor ($P < 0.0001$), shoulder dystocia ($P < 0.0001$), instrumental delivery ($P < 0.0001$), size of the ($P < 0.0001$), birth weight more than 3.5 kg ($P < 0.0001$). The maternal weight, sex of the baby, maturity of the baby does not predispose to birth trauma.

Table 4: Mode of delivery in birth trauma

Mode of delivery	Cases *n*=283 (%)	Controls *n*=366 (%)	*P*-value*
Normal	119 (42.05)	226 (61.75)	<0.0001
LSCS	109 (38.51)	134 (36.61)	
Instrumentation	55 (19.44)	6 (1.64)	

LSCS: Lower segment cesarean section, **P*<0.05 significant

Table 5: Birth weight in birth trauma

Birth weight (kg)	Cases *n*=283 (%)	Controls *n*=366 (%)	*P*-value*
<2.5	28 (9.9)	87 (23.77)	<0.0001
2.5-3.0	55 (19.43)	197 (53.83)	
3.0-3.5	139 (49.12)	76 (20.77)	
3.5-4.0	49 (17.31)	5 (1.37)	
>4	12 (4.24)	1 (0.27)	

**P*<0.05 significant

DISCUSSION

The incidence of birth trauma in this study was 22.22/1000 live births. The higher incidence found in our study is due to the fact that study place is a referral institution, where more number of high risk cases are delivered. Head and neck injuries were the most common with an incidence of 19.47/1000 live births in contrast Hughes *et al.*,[7] 1991-97 reported an incidence of 9.5/1000 live births in his study of Birth trauma in the head and neck. If subconjunctival hemorrhage excluded as done by Hughes *et al.*,[7] incidence of Birth trauma to head and neck was 11.78/1000 live births which is marginally higher. The Nerve injuries had an incidence of 1.1/1000 live births in our study. The incidence of nerve injuries in our study is comparable with study done by Padmini *et al.*,[8] in contrast other studies were marginally higher than the present study (1.61-2.34/1000 live births). The incidence of bone injuries in this study was 0.3/1000 live births. The bony injuries when compared with other studies, higher than the present study. The present study was showing 2-3 times reduction in the incidence of bony injuries than the older studies, may be due to the improved obstetrical care and selecting lower segment cesarean section as mode of delivery for high risk cases. The incidence of Skin and soft tissue injuries in this study is 0.13%. Both lower and higher incidence of soft tissue injuries were found when compared to the present study (0.04-0.32%). No case of intra abdominal injuries were recorded in this study which is comparable with studies done by Padmini *et al.*,[8] in contrast 0.09-0.33/1000 live births, intraabdominal injuries were found in other studies. The incidence of Cephalhematoma in our study was 0.57%. Other studies reported an incidence ranging from 0.12% to 2.5%.The incidence of subgaleal hemorrhage was 0.47/1000 live births in this study. Ng *et al.*,[9] 1990-1993 reported an incidence of 0.8/1000 live births. The reason for low incidence may be due to drastic reduction of vacuum deliveries, just 5 (1.6%) out of 321 instrumental deliveries. The incidence of brachial palsy in this study was 0.8/1000 live births. This was comparable to the study by Perlow *et al.*[4] Other studies incidence ranges from 0.27 to 2.6/1000 live births. The incidence of facial nerve palsy found in our study was 0.31/1000 live births. In contrast to this other studies report higher incidence of facial nerve palsy 0.6-8/1000 live births. Fracture femur incidence in our study was 0.16/1000 live births, which is comparable to the other studies. The incidence of fracture humerus in our study was 0.08/1000 live births, which is comparable to the study done by Al-Habdan[10] 0.1/1000 live births. The incidence of clavicle fracture in our study was 0.08/1000 live births, in contrast to other studies which report higher incidence, 0.46-2/1000 live births.

Predisposing Factors

Primiparity is the most common parity in the study group in our study, which is comparable to other studies even though each group differs. Nearly 95% of the mothers in study group were booked in our study, in contrast to 34.3% in Bhat *et al.*[11] Breech presentation was found in 8.13% of cases in our study, in contrast to Bhat *et al.*,[11] recorded 20% of breech presentation. Obstructed labor seen in 26.15% in our study, in contrast to 17% seen in study done by Hughes *et al.*[7] Normal delivery was the maximum mode of delivery in our study, which is comparable to Awari *et al.*[12] and Padmini *et al.*[8] in contrast Hughes *et al.*,[7] reported instrumentation as the predominant mode of delivery in the study group. The birth injuries were common among babies with birth weight more than 3.5 kg in our study which is comparable to study by Fabamwo *et al.*,[13] in contrast to western reports where birth injuries common in more than 4 kg babies. Even though incidence of birth trauma high in our study, when compared with other studies, there is actually reduction in mortality and major injuries such as nerve, bone, intra abdominal, and intra cranial injuries, just 30 (10.4%) of 288 injuries, all these may be due to the improvement in obstetrical care.

CONCLUSION

Primiparity was the most important risk factor. The presence of maternal obstetric risk factors like Malpresentation increases the incidence of birth trauma even in skilled and competent hands. Early referral from PHI may decrease birth trauma. Use of uterine stimulants, prolonged and obstructed labor, shoulder dystocia predisposes to birth trauma. Instrumental delivery, especially midforceps and vacuum extraction predispose to mechanical injuries. LGA and birth weight more than 3.5 kg are important risk factors. Most of the injuries are self limiting.

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Original Article

Feracrylum Versus Topical Adrenaline for Hemostasis in Tonsillectomy

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Abstract

Background: Primary hemorrhage is the most common and fatal complication of tonsillectomy.

Aims and Objectives: The study was to compare the efficacy of feracrylum and topical adrenaline in hemostasis.

Materials and Methods: A total of 40 patients were divided into two groups of 20 patients each. Feracrylum was used in one group and topical adrenaline in the other.

Results: Hemorrhage was lesser in the group where feracrylum was used.

Conclusion: Feracrylum is advisable to achieve hemostasis in tonsillectomy.

Key words: Complication, Hemorrhage, Tonsillectomy

INTRODUCTION

Tonsillectomy is one of the most common surgeries performed by otolaryngologists. Tonsillectomy is generally performed as an inpatient surgery because of concerns regarding post-tonsillectomy hemorrhage. Hemorrhage, which is a severe complication associated with this procedure, has been reported to occur in 2-4% of patients.[1] Furthermore, bleeding in the upper aerodigestive tract always represents a significant risk.[2] Primary bleeding is generally considered to be related to surgical technique, whereas environmental factors that influence oropharyngeal healing contribute to secondary hemorrhage. For primary hemostasis, two different techniques are mainly used, bipolar diathermy, and suture ligation. Suturing the faucial pillars is typically used in severe hemorrhage where other techniques have failed.[3]

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In this study, we intend to compare the use of gauze soaked in feracrylum with that of adrenaline pledgets.

Aims and Objectives

The study was to compare the efficacy of feracrylum with that of adrenaline in the management of primary hemorrhage in tonsillectomy.

MATERIALS AND METHODS

A total of 40 patients who underwent tonsillectomy in a tertiary care center from January 2016 to June 2016 were included in this study (Figure 1). They were divided into two groups of 20 patients each. Topical Adrenaline was used in one group and feracrylum in the other. Dissection and snare method was performed (Figure 2).

Inclusion Criteria

1. Age above 5 years
2. Chronic tonsillitis
3. Recurrent attacks of a sore throat.

Exclusion Criteria

1. Patients with bleeding diathesis
2. Acute exacerbation of chronic tonsillitis
3. Patients undergoing tonsillectomy for quinsy.

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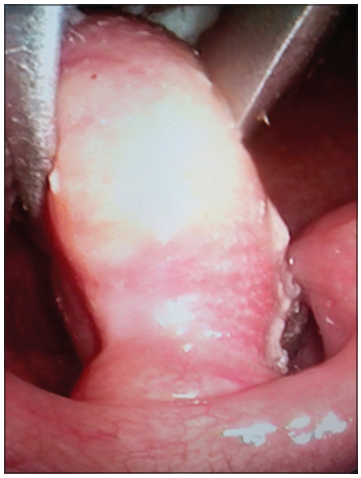

Figure 1: Tonsil being grasped

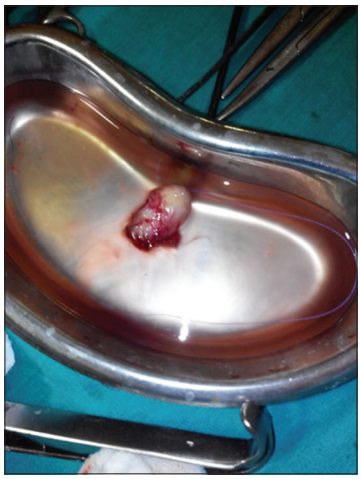

Figure 2: Tonsillectomy specimen

Table 1: Age distribution of patients who underwent tosillectomy

Age in years	Adrenaline (%)	Feracrylum (%)	Total (%)
<10	2 (10)	2 (10)	4 (10)
10-20	4 (20)	8 (40)	12 (30)
21-30	5 (25)	3 (15)	8 (20)
31-40	7 (35)	6 (30)	13 (32.5)
>40	2 (10)	1 (5)	3 (7.5)
Total	20 (100)	20 (100)	40 (100)
Mean±SD	26.95±11.88	21.70±12.26	24.33±12.01

Table 2: Sex distribution of patients who underwent tonsillectomy

Gender	Adrenaline (%)	Feracrylum (%)	Total (%)
Female	13 (65)	13 (65)	26 (65)
Male	7 (35)	7 (35)	14 (35)
Total	20 (100)	20 (100)	40 (100)

Table 3: Primary haemorrhage

Primary haemorrhage	Adrenaline (%)	Feracrylum (%)	Total (%)
Absent	14 (70)	20 (100)	34 (85)
Present	6 (30)	0 (0)	6 (15)
Total	20 (100)	20 (100)	40 (100)

Table 4: Ligation of vessels during tonsillectomy

Ligation of vessels	Adrenaline (%)	Feracrylum (%)	Total (%)
Not ligated	8 (40)	20 (100)	28 (70)
Ligated	12 (60)	0 (0)	12 (30)
Total	20 (100)	20 (100)	40 (100)

Observation

Age distribution

A total of 2 patients each were present in the age group of below 10 years. In the age group of 11-20 years, there were 4 patients in the adrenaline group and 8 patients in feracrylum group. In the age group of 21-30 years, there were 5 patients in the adrenaline group and 3 in feracrylum group. In the age group of 31-40 years, there were 7 patients in Adrenaline group and 6 in feracrylum group. In the age group of above 40 years, there were 2 patients in Adrenaline group and 1 in feracrylum group (Table 1).

Sex distribution

There were 13 female patients in both the groups and 7 male patients in both the group (Table 2).

Primary hemorrhage was present in 6 patients in adrenaline group (Table 3). Patients in the feracrylum group did not suffer from primary hemorrhage. $P = 0.02$ which was significant.

Bleeding vessels needed ligation in 12 patients belonging to adrenaline group (Table 4). Patients in the feracrylum group did not need ligation of vessels. $P < 0.001$ was also significant. Chi-square test was used.

DISCUSSION

Post-tonsillectomy hemorrhage remains the most serious and even fatal complication of tonsillectomy. Minor bleeding does not require any active measures, but major bleeding necessitates control of hemorrhage under general anesthesia in the operation theater. Hemostasis is usually secured by ligating the bleeders or coagulating them by diathermy, or by a combination of both of these. Primary hemorrhage generally occurs due to surgical technique. Secondary hemorrhage occurs due factors that influence wound healing. Most cases of fatal post-operative bleeding occur within the first 24 h after surgery. Mortality rate due to post-tonsillectomy hemorrhage is 2 in 10000 tonsillectomies. Post-operative monitoring of at least 6 h postsurgery is recommended in literature.[3]

Tong *et al.* did not report a single case of primary hemorrhage in their study of 90 tonsillectomies.[4] Anwar *et al.* concluded

that suture ligation and coagulation diathermy are equally effective in the management of primary hemorrhage.[3] Robb *et al.* concluded that perioperative use of tranexamic acid reduces primary hemorrhage.[5] Senska *et al.* advocated suturing of tonsillar pillars to reduce primary hemorrhage.[2] Clark *et al.* concluded that incidence of post-tonsillectomy hemorrhage is more in adults than children.[6]

Feracrylum is a novel hemostatic agent. It is used in control of oozing in many of the surgeries. It decreases post-operative wound infection as it has antimicrobial properties. It activates thrombin which subsequently causes conversion of fibrinogen to fibrin which leads to clot formation. When it comes in contact with serum proteins, it forms a thin film which acts as a mechanical barrier preventing exogenous contamination. Feracrylum has a molecular weight of 500000-800000 Daltons, thus has no systemic absorption and no adverse effects on kidney, liver, cardiovascular, and hemopoietic systems.[7]

The previous studies have not mentioned the use of feracrylum in reducing post-tonsillectomy hemorrhage.

CONCLUSION

Use of feracrylum in tonsillectomy reduces the post-operative hemorrhage significantly. As it has antimicrobial property, it reduces the incidence of secondary hemorrhage also.

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Original Article

Comparative Study of Stone Free Rate, Morbidity and Need for Retreatment Procedures between Various Surgical Modalities for 10-20 mm Upper Urinary Tract Calculi

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Abstract

Introduction: The constant technological refinement in the field of minimal invasive treatment modalities of endourology influences their efficacy and the associated morbidity. Added to this are the surgeons' ability to learn and adapt to the changing technology that in turn has a significant impact on the final outcome.

Materials and Methods: The study is a prospective observational comparative study conducted in a single institution over 1-year period from November 2013 to October 2014. A total of 287 cases of renal and upper ureteric calculi of 10-20 mm size were included in the study.

Results: A total of 287 patients were included in our study over 1-year. This included 161 cases of percutaneous nephrolithotomy (PCNL), 45 of retrograde intrarenal surgery (RIRS), and 81 of shockwave lithotripsy (SWL). The mean age was 43.69 years with a median of 42 years. There were 202 males and 85 females in our study, with a male:female ratio of 2.38:1. The mean stone size in PCNL, RIRS, and extracorporeal SWL groups were 14.73, 13.84, and 13.52 mm, respectively. The overall success rate with respect to stone clearance was 88.9% (*n* = 255) and the failure rate was 11.1% (*n* = 32). An average of 12.5% of patients had residual stones, with the maximum seen in SWL (17.3%). Nearly, one-fifth of the patients who had SWL done and needed retreatment.

Conclusions: PCNL and RIRS have comparable success and complication rate, whereas SWL has lower complication rate. When comparing the stone free rate PCNL and RIRS are better. Thus, tailoring the management with respect to the patient, stone and other technical factors with respect to better stone free rate is needed.

Key words: Lithotripsy, Nephrolithotomy, Percutaneous, Steinstrasse, Ureterorenoscopy, Urolithiasis

INTRODUCTION

The primary goal while treating renal calculi and upper ureteric calculi is to achieve maximum clearance of stone with minimal morbidity. The various minimally invasive modalities described are extracorporeal shockwave lithotripsy (ESWL), percutaneous nephrolithotomy (PCNL), and retrograde intrarenal surgery (RIRS).[1,2] The other modalities in the management of these stones are open and laparoscopic nephrolithotomy or pyelolithotomy, which are more invasive. The preferred approach for stones <1 cm is SWL, whereas for stones >2 cm, it is PCNL, but the management of stones of 1-2 cm is still controversial.[3] Addition of RIRS to the armamentarium in the last two decades has added to the dilemma. The constant technological refinement in the instruments of

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the minimal invasive treatment modalities influences their efficacy and the associated morbidity. Added to this are the surgeons ability to learn and adapt to the changing technology, impacts the outcome. Hence, there is a need to re-evaluate the relative roles and efficacies of these treatment modalities from time to time. This study is an attempt to compare the three modalities available for the treatment of upper urinary tract calculi.

Aim

To compare SWL, PCNL, and RIRS in the management of renal and upper ureteric calculi above L4 transverse process of 10-20 mm size in terms of stone-free rate, morbidity and need for retreatment procedures. The various parameters such as success rate, retreatment rate, need for an auxiliary procedure, complication rate, mean Procedure time, and mean hospital stay are taken into consideration during this study.

MATERIALS AND METHODS

The study is a prospective observational comparative study conducted in a single institution over 1-year period from November 2013 to October 2014. A total of 287 cases of renal and upper ureteric calculi of 10-20 mm size were included in the study. These patients underwent PCNL, RIRS or SWL. The study model was presented to the Ethical Committee of the institute and was approved.

Inclusion and Exclusion Criteria

The inclusion criteria were all patients presenting with calculi of 10-20 mm in otherwise normal renal pelvicalyceal system, pelvi-ureteric Junction or proximal ureter up to L4 transverse process. The exclusion criteria included all stones identified distal to L4 transverse process, multiple renal calculi with second calculi size >4 mm, abnormal upper urinary tract anatomy such as duplex system, horseshoe kidney, ectopic kidney, and pelvi-ureteric junction obstruction, any axial skeletal abnormality such as scoliosis and kyphosis, and associated bleeding diathesis.

An elaborate history and physical examination were done. The imaging modalities used for the diagnosis consists of one or more of the following and includes ultrasonography, X-ray KUB, and noncontrast computed tomography KUB with or without contrast. In addition, the patients also underwent the relevant blood and urinary investigations such as hemoglobin, renal function test, and coagulation profile.

Choice of Procedure

The choice of treatment modality for the management of the upper urinary tract calculi of 10-20 mm calculi is largely determined by the individual surgeon taking into consideration the patients' anatomy, comorbid conditions, urinary tract anatomy, the stone density, and location as well as patients preference. PCNL and RIRS with flexible ureterorenoscope were done under general anesthesia. ESWL was done under intravenous sedation. Following the procedure, the patient undergoes ultrasonography and X-ray KUB in the 2nd post-operative day and at 2 weeks and 6 weeks with ultrasonography and X-ray KUB. Complications from each group were categorized as minor and major.

Statistical Methods

Descriptive statistical analysis was performed in this study. To describe the data frequency analysis, percentage analysis were used for categorical variables and for continuous variables the mean and standard deviation (SD) were used. For the multivariate analysis, the Kruskal–Wallis test and ANOVA were used and for trivariate and bivariate analysis Mann–Whitney test was used. To find the significance in categorical data, Chi-square test was used. The $P < 0.05$ is considered as significant level. The statistical software SPSS 16.0 version was used for the analysis of the data and Microsoft Word and Excel have been used to generate figures and tables.

RESULTS

A total of 287 patients were included in our study over 1-year. This included 161 cases of PCNL, 45 of RIRS, and 81 of SWL. The mean age was 43.69 years, with a median of 42 years and a standard deviation of 13.275. The minimum age was 18 years, with one male child, who was aged 10 years was also included in our study (Figure 1). There were 202 males and 85 females in our study, with a male:female ratio of 2.38:1. The right and left sides were almost equally affected by the stone disease, with the left kidney slightly more commonly affected than the right. Table 1 gives the demographic details of the number, mean

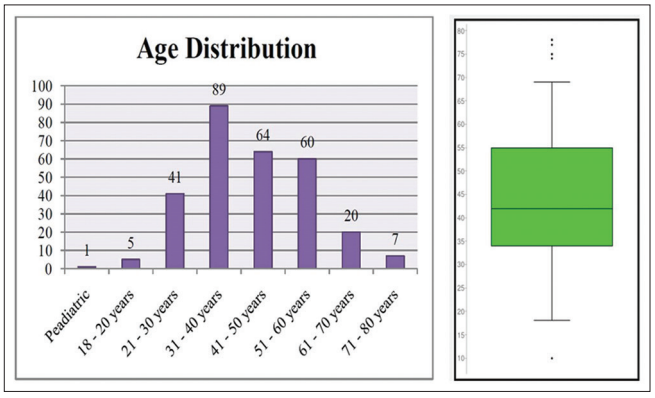


Figure 1: Graphical and box plot representing the age distribution

age distribution, sex ratio, and the laterality of renal stone disease in our study.

The mean stone size in PCNL, RIRS, and ESWL groups were 14.73, 13.84, and 13.52 mm, respectively. The overall mean stone size was 14.25 mm with an SD of 2.881. The mean stone size of RIRS group was comparable with that of PCNL group as well as SWL group. However, the mean stone size of PCNL group was statistically different which is bigger than ESWL group even though the actual mean difference was only 1.21 mm ($P = 0.009$) (Table 2). Whereas the average time taken for the procedure is fairly constant with SWL, for PCNL and RIRS it was 81 and 85 min, respectively. PCNL and RIRS took a statistically significantly longer time in comparison to SWL (Table 2). The average duration of hospital stay was significantly longer for PCNL and RIRS in comparison to SWL (Table 2). While most of the ESWL was done as a day care procedure, a few of them needed inpatient care in view of health-care insurance or co-existing comorbidities and hence the average duration of hospital stay in this subgroup was 1.21 days.

The overall success rate with respect to stone clearance was 88.9% ($n = 255$), and the failure rate was 11.1% ($n = 32$).

Table 1: Demographic details of cases in our study

Demographic details	PCNL	RIRS	SWL	Total	*P*-value
Total number of cases	161	45	81	287	-
Mean age (in years)	45	40.56	42.96	43.73	0.138
Sex					
Male	114	37	51	202	0.075
Female	47	8	30	85	
Laterality					
Right	82	23	31	136	0.152
Left	79	22	50	151	
Failure rate	16/161	6/45	14/81	36/287	0.796

PCNL: Percutaneous nephrolithotomy, RIRS: Retrograde intrarenal surgery, SWL: Shockwave lithotripsy

Table 2: Stone size, duration of procedure and mean stay period in hospital

Group	*n*	Mean±standard deviation	Chi-square test	*P*-value
Mean stone size (in mm, longest diameter)				
PCNL	161	14.73±3.066	9.338	0.009
RIRS	45	13.84±2.449		
SWL	81	13.52±2.545		
Total	287	14.25±2.881		
Procedural time (in min)				
PCNL	161	81.34±30.902	129.402	0.0005
RIRS	45	84.89±29.358		
SWL	81	45±0.000	Kruskal–Wallis test	
Mean duration of stay in hospital (in days)				
PCNL	161	4.61±1.189	183.315	0.0005
RIRS	45	3.49±1.424		
SWL	81	1.21±0.754	Kruskal–Wallis test	

PCNL: Percutaneous nephrolithotomy, RIRS: Retrograde intrarenal surgery, SWL: Shockwave lithotripsy

Table 1 gives the details of the failure rates with each of the procedures. However, there was no significant difference between the failure rates between the two sides. Table 3 gives details of the failure rate with respect to the stone location.

Table 4 and Figure 2 provide the details of the residual fragments after the three procedures. A residual fragment of more than 4 mm is considered to be a significant residual fragment. An average of 12.5% of patients had residual stones, with the maximum seen in SWL (17.3%), closely followed by RIRS in 13.3%. However, the numbers are not statistically significant.

Table 4 also provides details regarding the number of patients who needed retreatment. Nearly, one-fifth of patients who had SWL done and needed retreatment. One patient who had RIRS needed a relook ureteroscopy, as after the initial procedure there was bleeding. Relook RIRS was done 3 weeks after double J-stenting. Nine patients in the PCNL group and five from RIRS group needed SWL. However, none of the patients in the SWL group needed any other auxiliary procedure (Table 4).

Table 5 gives the details of the residual stones at 2 weeks and 6 weeks following the procedure. At 2 weeks, the residual calculi noted following the primary procedure was analyzed but are not statistically significant with all three groups. However, clinically SWL has the maximum number of patients (17.3%) with significant residual calculi at the end of 2 weeks needing auxiliary procedures. When reviewed at the end of 6 weeks following auxiliary procedures, all the patients are stone free in all 3 groups.

RIRS was associated with maximum percentage of complications. Table 6 illustrates the list of complication associated with each of these procedures. When comparing the various complications between groups, the values

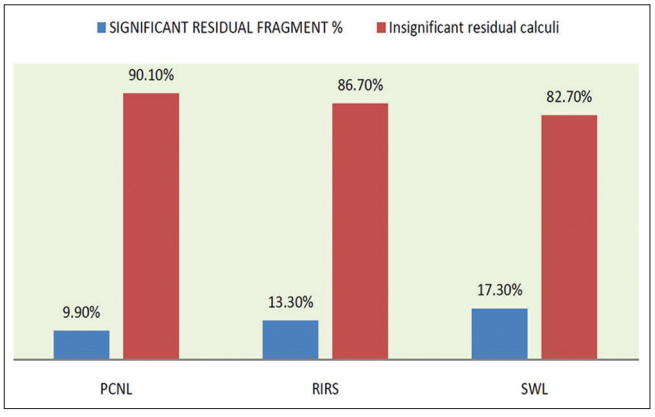


Figure 2: Comparison of significant and insignificant residual fragments

Table 3: Location of stones

Procedure	Upper calyx		Middle calyx		Lower calyx		Renal pelvis		Upper ureter	
	Number	Failure	Number	Failure	Number	Failure	Number	Failure	Number	Failure
PCNL	25	6	42	2	35	1	42	7	17	0
RIRS	9	0	2	0	5	1	5	0	24	5
SWL	33	4	2	2	0	0	22	2	5	2
P-value	0.0005		0.0005		0.0005		0.0005		0.0005	

PCNL: Percutaneous nephrolithotomy, RIRS: Retrograde intrarenal surgery, SWL: Shockwave lithotripsy

Table 4: Residual fragments, retreatment rate and auxiliary procedures in each group

Variables	Groups (%)			Total	Chi-square test	*P*-value
	PCNL	RIRS	SWL			
Residual fragments						
No fragments	145 (90.1)	39 (86.7)	67 (82.7)	251 (87.5)	2.681	0.262
Fragments present	16 (9.9)	6 (13.3)	14 (17.3)	36 (12.5)		
Retreatment						
No retreatment required	154 (95.7)	44 (97.8)	65 (80.2)	263 (91.6)	47.609	0.0005
SWL	0	0	16 (19.8)	16 (5.6)		
Flexible ureteroscope	0	1 (2.2)	0	1 (0.3)		
Redo PCNL	7 (4.3)	0	0	7 (2.4)		
Auxiliary procedure						
No auxiliary procedure	152 (94.4)	40 (88.9)	79 (97.5)	271 (94.4)	13.018	0.011
ESWL	9 (5.6)	5 (11.1)	0	14 (4.9)		
Ureteroscopy	0	0	2 (2.5)	2 (0.7)		

PCNL: Percutaneous nephrolithotomy, RIRS: Retrograde intrarenal surgery, SWL: Shockwave lithotripsy, ESWL: Extracorporeal shock wave lithotripsy

Table 5: Residual fragments at 2 weeks and 6 weeks after surgery

Residual fragments	Groups (%)			Total	Chi-square test	*P*-value
	PCNL	RIRS	SWL			
At the end of 2 weeks						
No residual fragments present	145 (90.1)	39 (86.7)	67 (82.7)	251 (87.5)	2.681	0.262
Significant residual fragments present	16 (9.9)	6 (13.3)	14 (17.3)	36 (12.5)		
At the end of 6 weeks						
No residual fragments present	161 (100)	45 (100)	81 (100)	287 (100)	0	

PCNL: Percutaneous nephrolithotomy, RIRS: Retrograde intrarenal surgery, SWL: Shockwave lithotripsy

Table 6: Complication rates in each group

Complications	Groups (%)			Total (%)	Chi-square test	P-value
	PCNL	RIRS	SWL			
No complication	149 (92.5)	40 (88.9)	75 (92.6)	264 (92)	19.641	0.033
Bleeding	11 (6.8)	3 (6.7)	2 (2.5)	16 (5.6)		
False passage	0	1 (2.2)	0	1 (0.3)		
Hematoma	0	0	2 (2.5)	2 (0.7)		
Perforation	1 (0.6)	1 (2.2)	0	2 (0.7)		
Steinstrasse	0	0	2 (2.5)	2 (0.7)		
Groups			*P*-value			
PCNL versus RIRS			0.677			
PCNL versus SWL			0.804			
RIRS versus SWL			0.751			

PCNL: Percutaneous nephrolithotomy, RIRS: Retrograde intrarenal surgery, SWL: Shockwave lithotripsy

are statistically significant ($P = 0.033$). When assessing individually the RIRS group has a maximal complication rate with 11.1% compared with PCNL and SWL groups which were 7.4% and 8.0%, respectively.

On assessing, the overall success rate of the three modalities, a residual fragment of ≤4 mm following the procedure is considered as the success of the primary procedure. On assessing the groups, PCNL has the maximum success rate

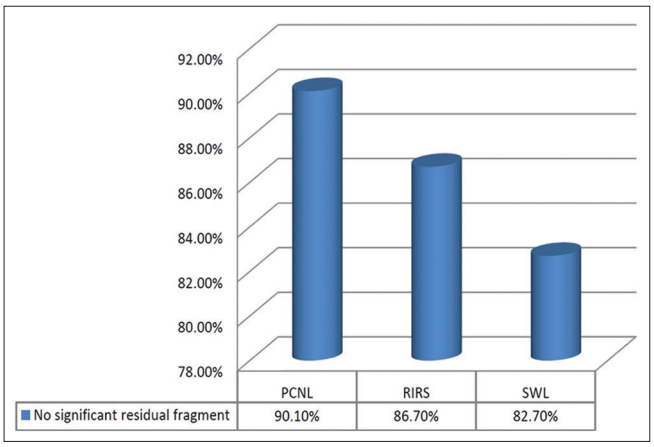
with 90.1% cases while RIRS has 86.7% and SWL has the least success rate of 82.7% (Figure 3).

DISCUSSION

The term endourology was defined as a closed controlled manipulation within the genitourinary tract.[1] The development of minimally invasive surgical techniques for treating renal stones has largely revolutionized due to various technologic advances in the fiber optics, better radiographic imaging, and various types of lithotripsy modalities (pneumatic, ultrasonic, electrohydraulic, and laser) available these days. All these developments redefined the modern techniques of stone removal, including ESWL, flexible ureteroscopy, and PCNL.

The factors determining which type of management suits a particular patient depends on various factors associated with the stone, anatomy of kidneys, and patient related issues. The stone factors include their number, size, and composition. Renal anatomic factors are the presence of obstruction, degree of hydronephrosis, location of the stone, and associated anomalies such as pelvi-ureteric junction obstruction, renal ectopia or fusion, calyceal diverticulum, and horseshoe kidney, as all these can hinder stone clearance after SWL. The patient related factors include age, obesity, body habitus and deformity, presence of infection, hypertension, renal failure, and associated coagulopathy.

Stone burden plays an important role in the treatment decision. For patients with nonstag horn stones of size lesser than 10 mm, SWL is the primary modality. For patients with size between 10 and 20 mm, SWL can still be considered even though successful outcome may be achieved with other modalities. Patients with stones of size larger than 20 mm should ideally be managed by PCNL unless specific indications for ureteroscopy are present like



Figurer 3: Overall success rate of study groups

obesity or bleeding diathesis.[2-4] SWL results vary inversely with stone burden whereas PCNL stone free rates were largely independent of stone burden.[5]

Lingeman reported the influence of composition when adjusted for size of the stone. Cystine, brushite calculi, and calcium oxalate monohydrate appeared more resistant to SWL, followed in descending order of resistance by struvite, calcium oxalate dihydrate, and uric acid stones.[6] Hence, SWL should be offered with great caution in such patients only when the stone size is <1.5 cm.[7,8] Wang *et al.* confirmed that stone density higher than 900 HU is a predictor of a poor SWL outcome.[9] El-Nahas *et al.* also found that a stone density more than 1000 HU predicted failure after SWL.[10] Khalil studied 438 patients with stones of size 1 cm, 1.1-2 cm and more than 2 cm and concluded that stone burden rather than stone location is the most important predictor of SWL outcome.[11]

Our study helps to compare SWL, PCNL, and RIRS in the management of renal and upper ureteric calculi above L4 transverse process of 10-20 mm size in terms of stone free rate, morbidity experienced by the patient on the completion of the treatment. In the PCNL group of the 161 patients who underwent the procedure, the laterality was more or less equal with 5.6% failure seen on left side when compared to right which is 4.3%. Even though the difference is small and insignificant, this predominant left sided failure may be due to the highly placed left kidney, which needs further validation. The average size of the stone was 13.84 mm with 13.3% having residual calculi following primary procedure thus needing a second procedure. When comparing the failure with location of the stone, upper ureteric calculi have the maximum failure 11.1% followed by lower calyceal calculi (2.2%). This can be explained because of difficulty in using a flexible ureterorenoscopy in a non-stented ureter following up migration of the stone proximally. However, the same authors had later on started doing pushback PCNL for such upper ureteric stones, claiming a much higher success rate.[12]

In our study, the mean stone size in each group was 14.73 mm for PCNL group and 13.84 mm and 13.52 mm in RIRS, and SWL group, respectively. Resorlu *et al.* revealed that the mean stone size for the PCNL group was a little higher with 17.3 mm and 15.6 mm for RIRS and 14.9 mm for SWL group.[13] In both studies, the mean stone size was statistically significant. PCNL had a success rate of 90.1% in our study at 2 weeks from the procedure. Similarly with RIRS and SWL, the success rates were 86.7% and 82.7%, respectively. On the other hand, Resorlu *et al.* showed good result with PCNL of 91.4% success while SWL had only 66.5% success on review post procedure requiring auxiliary procedure for complete stone clearance. Akman

et al., compared PCNL with RIRS, showing better success with PCNL (92.8%) compared with RIRS (82.1%).[14] Cecen *et al.* compared RIRS with SWL showing better results with RIRS (92% vs. 87%).[15] Nearly, 17.3% patients in SWL group needed retreatment with the same modality that required to undergo 2nd and 3rd sitting SWL for the residual calculi. Resorlu *et al.* group had a retreatment of 21.9% for SWL group, and in Cecen *et al.* study, the retreatment rate with SWL was 12.9% (Table 7).

Table 7 also compares the outcomes of various studies with regard to stone free rates, mean hospital stay, and complication rates. From our study, the mean hospital stay for PCNL was 4.61 days and least for SWL as it is mostly done as day care procedure. Resorlu *et al.* published his results where the mean stay in hospital was 2.6 days for PCNL and 1.3 days for RIRS. SWL was done as an outpatient procedure. Carlsson *et al.* observed that post PCNL patients stayed for 7.4 days when compared to SWL patients, where the mean hospital stay was 4.1 days.[16] The need for such a prolonged stay in the hospital and an inpatient care in SWL group is debatable. Carlsson *et al.*, observed that one of the reasons for inpatient treatment was to standardize the management of patients in the ESWL unit. According to their observation, this routine practice also facilitates a high patient turnover, which reduces the cost per session. Akman *et al.* noted an average of 2.8 days in PCNL group and 1.2 days for RIRS patients.[14] Table 7 also illustrates the comparison of overall complication rate between various studies. In our study, it was high in RIRS group with 11.1% while PCNL group had 7.4% and SWL group had 9.9%. All complications reported were minor. Resorlu *et al.* published his complication rate with 20% in PCNL group. The decision to offer SWL for moderately sized stones was also biased because of the higher percentage of complications. However, we observed that as learning curve improves, with time and in well-experienced hands, PCNL can achieve a maximal success outcome with minimal morbidity.

Limitations of Our Study

Our sample size is small and associated difficulty with performing statistical analysis. Moreover, there is a variable *n* value in the study groups. The study was unable to exclude many of the other confounding factors which may have influenced some of the outcomes analyzed which is beyond the scope and purview of this study. However, further studies with larger sample size and after elimination of confounding factors would have been ideal and are recommended.

CONCLUSION

PCNL and RIRS have comparable success and complication rate, whereas SWL has lower complication rate. When comparing the stone free rate, PCNL, and RIRS are better than SWL. More number of cases needed auxiliary procedures in SWL patients. Thus, tailoring the management with respect to the patient, stone parameters, and other technical factors is needed to achieve a good stone clearance with least morbidity. In the case of PCNL, the complications can be reduced using smaller nephroscope and smaller tract dilatation, but its invasiveness is always a cause for

Table 7: Comparison with various other similar studies

Group	Our study	Resorlu study	Cecen *et al.* study	Akman *et al.* study	Others
Stone free rate (%)					
PCNL	90.1	91.4	-	92.8	-
RIRS	86.7	87.0	92	82.1	-
SWL	82.7	66.5	87	-	-
Retreatment rate (%)					
PCNL	4.3	5.7	-	0	
RIRS	2.2	8.7	0	17.9	
SWL	17.3	21.9	12.9	-	
Need for auxiliary procedures (%)					
					Albala *et al.*, 2001
PCNL	5.6	5.7	-	-	1.72
RIRS	11.1	8.7	0	-	-
SWL	19.8	21.9	12.9	-	15.63
Duration of mean hospital stay (Days)					
					Carlsson *et al.*
PCNL	4.61	2.6	-	2.8	7.4
RIRS	3.49	1.3	-	1.2	-
SWL	1.21	0	-	-	4.1
Complication rate (%)					
PCNL	7.4	20.1	-	10.7	
RIRS	11.1	10.9	7.5	7.1	
SWL	9.9	7.6	6.4	-	

PCNL: Percutaneous nephrolithotomy, RIRS: Retrograde intrarenal surgery, SWL: Shockwave lithotripsy

great concern. In the case of RIRS, the stone can be managed endoscopically, but prestenting the patient before RIRS can improve the easy manoeuvrability of flexible ureterorenoscopy, thus reducing the failure rate and showing comparable success to PCNL. The reduced stone free rate of SWL can be pointed to the efficacy of the technician performing the procedure and also the quality of the hardware. RIRS will be a better modality for the treatment of upper urinary tract calculi of size 10 – 20 mm provided all patients were stented before RIRS when comparing the invasiveness of PCNL and higher retreatment and failure rate of SWL.

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Original Article

Magnesium Levels in Diabetes Mellitus: A Prospective Study

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Abstract

Background: The prevalence of retinopathy is strongly related to the duration of diabetes. After 20 years of diabetes, nearly all patients with Type 1 diabetes and >60% of patients with Type 2 diabetes have some degree of retinopathy. Diabetic retinopathy which poses a serious threat to vision should be diagnosed at an earlier stage.

Objective: The aim was to study diabetic patients and derive a relation or role of serum magnesium and glycosylated hemoglobin (HbAlc) levels in diabetic retinopathy.

Materials and Methods: A total of 100 patients who were admitted and fulfilled the inclusion/exclusion criteria were evaluated by history, physical examination, and lab tests.

Results: Serum magnesium levels are compared in the 2 groups. The mean serum magnesium level in Group 1 is 2.01 with a standard deviation of 0.28. In Group 2, the mean level is 1.86 with a standard deviation of 0.40. Using paired *t*-test, the *P* value was calculated which came to be 0.035. A value <0.05 is considered significant. Glycosylated levels are compared in the 2 groups in the study. The mean HbAlc level in Group 2 is 8.8 with a standard deviation of 2.06, while the mean HbAlc level in Group 1 is 8 with a standard deviation of 1.99. Paired *t*-test was used to calculate the *P* value.

Conclusion: Thus, from the *P* value, we can suggest that there is a significant correlation between serum magnesium level and diabetic retinopathy and hence a role of magnesium in diabetic retinopathy can be proved, and A *P* = 0.011 is derived which shows that there is a significant correlation between glycosylated hemoglobin and diabetic retinopathy. Thus, glycosylated hemoglobin can be implicated in the pathogenesis of diabetic retinopathy.

Key words: Diabetes mellitus, Diabetic retinopathy, Glycosylated hemoglobin, Magnesium, Microvascular changes

INTRODUCTION

Diabetes is one the most common non-communicable disease worldwide and has become one of the leading causes of death in most developed countries. Diabetes and its complication "diabesity" is the price paid due to increase in the life-expectancy coupled with concomitant increase in dietary affluence and decrease in physical activity.

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Today "diabetegras" (which refers to Type 2 diabetes mellitus [DM]) accounts for more than 95% of all cases of diabetes worldwide. In comparison "diabete maigre" (which refers to Type 1 DM) is seen in a small number of cases.

Type 2 DM is one of the major contributors of mortality and morbidity and has a marked social, psychological and economical implication, thus creating much interest in the medical fraternity.

It is estimated that more than 300 million people will have diabetes by 2025. India has the dubious distinction of having the maximum number of diabetics in the world which stands at 44 million today. Hence, India is called the "diabetic capital of the world."

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Aretacus of Alexandria described diabetes as "to pass through" while Shushruta of India called it large volumes of sweet urine." The understanding of the disease was in the infant stage in the 19th century after which the course and complications of the disease were better recognized.

Doctors in the 19th century were therapeutically impotent, the main role being as those who describe symptom complexes and the natural history of the disease.

The long duration of diabetes is associated with both micro- and macrovascular compilations. Diabetic retinopathy is a highly specific vascular complication of both Type 1 and Type 2 diabetes. Eduard von Jaeger is credited with the first description of diabetic retinopathy in his "atlas of disease of the ocular fundus." In 1879,[1] Stephen Mackenzie and Sir Edward Nettleship found microaneurysms in flat preparations of the retina. Nettleship went on to identify new vessels and the beaded appearance of the retinal veins.[2] The full picture of diabetic retinopathy was described in 1890 by Julius Hirschberg and classified into three types. "Central punctuate diabetic retinitis" (characterized by spots and hemorrhages). "Hemorrhagic" and "pigmentary."[3] Hirschberg was the first to claim that this retinopathy was specific to diabetes.

The prevalence of retinopathy is strongly related to the duration of diabetes. After 20 years of diabetes, nearly all patients with Type 1 diabetes and >60% of patients with Type 2 diabetes have some degree of retinopathy diabetic retinopathy poses a serious threat to vision.

In the Wisconsin Epidemiologic Study of Diabetic Retinopathy, 3.6% of younger-onset patients (aged <30 years at diagnosis, an operational definition of Type 1 diabetes) and 1.6% of older-onset patients (aged >30 years at diagnosis, an operational definition of Type 2 diabetes) were legally blind. In the younger-onset group, 86% of blindness was attributable to diabetic retinopathy. In the older-onset group, where other eye diseases were common, one-third of the cases of legal blindness were due to diabetic retinopathy. Overall, diabetic retinopathy is estimated to be the most frequent cause of new cases of blindness among adults aged 20-74 years.

Aims and Objectives

- To show a correlation between magnesium and diabetic retinopathy.
- To study the possible role of low magnesium in the microvascular change in DM leading to retinopathy.
- To study the role of glycosylated hemoglobin in diabetic retinopathy.

MATERIALS AND METHODS

The aim was to study diabetic patients and derive a relation or role of serum magnesium and glycosylated hemoglobin levels in diabetic retinopathy.

The study comprised 100 diabetic patients that were seen in the outpatient department or admitted in tertiary care hospital.

The patients were divided into 2 groups depending on the presence of absence of diabetic retinopathy.

The control group (Group A) consisted of 50 patients who are diabetic and without any diabetic retinopathy changes. Out of 50 patients, 17 are male and 33 are female.

The control group (Group B) consisted of 50 patients who are diabetic with diabetic retinopathy changes. Out of 50 patients, 29 are male and 21 are female.

The diagnosis of DM is made by standard criteria recommended by American Diabetes Association (ADA).

Inclusion Criteria

Diagnosed diabetic cases on regular treatment with oral hypoglycemic agents or insulin or both.

Exclusion Criteria

1. Hypertension
2. Chronic diarrhea
3. Alcoholism
4. Chronic use of diuretics
5. Reduced renal function.

Diabetic retinopathy was assessed using direct and indirect ophthalmoscopy. Serum magnesium levels were done on automated Dade Behring machine. Glycosylated levels were done by Nycocard kits, which is a boronate affinity assay.

RESULTS

In this study, out of 100 patients, 46 are male and 54 are female. In Group 1, out of 50 patients, 17 are male and 33 female, while in Group 2, 29 are male and 21 are female (Tables 1 and 2).

Out of the 100 patients, 10 are below 40 years of age, 18 are between 41 and 50 years, 35 are between 51 and 60 years, 34 are between 61 and 70 years, and 3 are above 70 years. The maximum prevalence of diabetes was seen in between the ages 51 and 70 years which signifies age as an important risk factor for diabetes (Table 3).

Family history is a well-known risk factor of diabetes. In my study, out of 100 patients, 40 patients had a family history of diabetes in either father, mother, brother, sister, and grandfather or grandmother while 60 patients did not have a family history of diabetes (Table 4).

Table 1: Gender wise: Distribution of 100 patients with diabetes mellitus±retinopathy

Gender	Group 1	Group 2
Male	17	29
Female	33	21
Total	50	50

P=0.33, Chi-square test

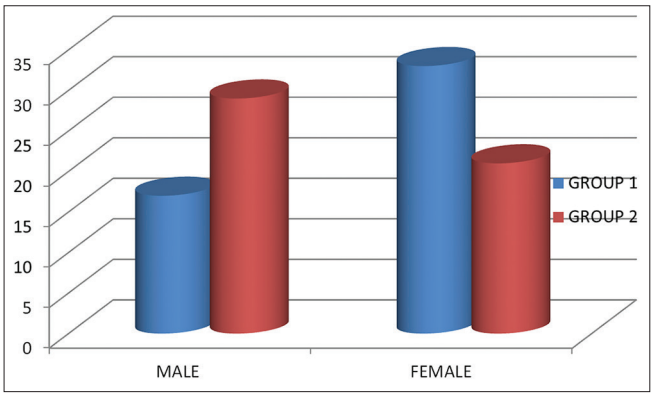
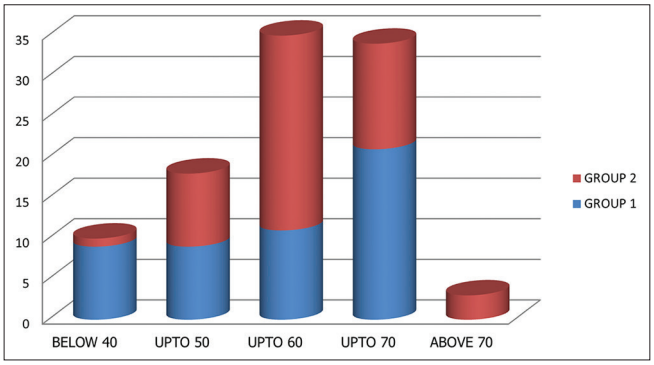


Table 2: Distribution of patients according to age group

Age (years)	Group 1	Group 2
Mean	54.1	57.5
Standard deviation	12.1	9.4
Range	29.70	38-80
Total	50	50

Age (years)	Group 1	Group 2	Total
Below 40	9	1	10
Up to 50	9	9	18
Up to 60	11	24	35
Up to 70	21	13	34
Above 70	0	3	3
Total	50	50	100

P=0.11, Paired *t*-test



Serum magnesium levels are compared in the 2 groups. The mean serum magnesium level in Group 1 is 2.01 with a standard deviation of 0.28. In Group 2, the mean level is 1.86 with a standard deviation of 0.40. Using paired *t*-test, the *P* value was calculated which came to be 0.035. A value <0.05 is considered significant. Thus, the from the *P* value, we can suggest that there is a significant correlation

Table 3: Distribution of patients according to number of diabetic years

Number of diabetic years	Group 1	Group 2	Total
Below 5	18	8	26
Up to 10	23	18	41
Up to 20	7	16	23
Up to 30	2	6	8
Above 30	0	2	2
Total	50	50	100

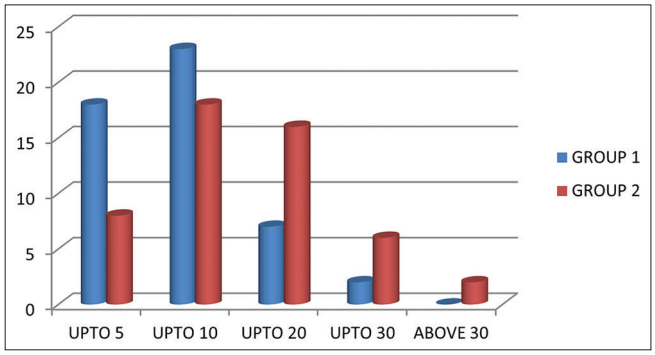
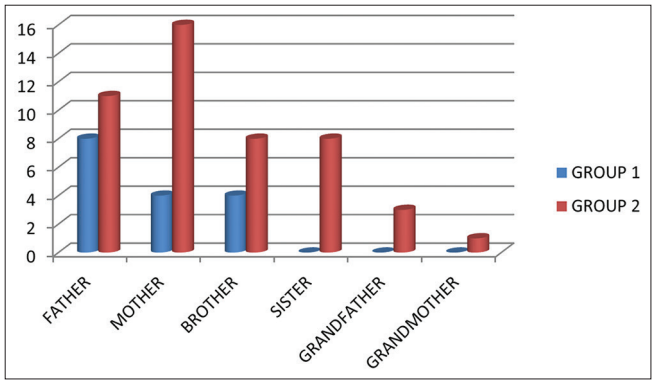


Table 4: Distribution of patients according to family history of diabetes

Family history	Group 1	Group 2	Total
Father	8	11	19
Mother	4	16	20
Brother	4	8	12
Sister	0	8	8
Grandfather	0	3	3
Grandmother	0	1	1
None	38	22	60
Total	50	50	100



between serum magnesium level and diabetic retinopathy and hence a role of magnesium in diabetic retinopathy can be proved (Table 5).

Glycosylated levels are compared in the 2 groups in the study. The mean glycosylated hemoglobin (HbAlc) level in Group 2 is 8.8 with a standard deviation of 2.06 while the mean HbAlc level in Group 1 is 8 with a standard deviation of 1.99. Paired *t*-test was used to calculate the *P* value. A $P = 0.011$ is derived which shows that there is a significant correlation between glycosylated hemoglobin and diabetic retinopathy. Thus, glycosylated hemoglobin can be implicated in the pathogenesis of diabetic retinopathy (Table 6).

Fasting sugar level is compared between the 2 groups. A mean FBS of 191.1 is seen in Group 2 with a standard deviation of 93.3 versus a mean level of 155.8 in Group 1 with a standard deviation of 48.8. The $P = 0.02$ by paired *t*-test which is significant showing the significance of elevated fasting sugar levels and occurrence of diabetic retinopathy (Table 7).

Postprandial sugar levels in the 2 groups are compared and a $P = 0.11$ is derived which shows there is no significant correlation between postprandial sugar levels and diabetic retinopathy (Table 8).

Serum creatinine levels are higher in Group 2 as compared to Group 1 with mean value of 0.88 with standard deviation of 0.23 in Group 1 and a mean value of 1.2 with a standard deviation of 1.04 in Group 2. The calculated $P = 0.0086$ is significant establishing a correlation between diabetic retinopathy and serum creatinine levels (Table 9).

In Group 1 (above) and Group 2 (below), the serum magnesium levels were compared with serum creatinine levels. A regression plot was made for their comparison. Since the values in both the graphs fall within the 95% confidence interval a straight line is plotted and no significant correlation is established between the two (Table 10).

Table 5: Comparison of serum magnesium levels in diabetics without retinopathy (Group 1) with diabetic with retinopathy (Group 2)

Serum magnesium	Group 1	Group 2
Mean	2.01	1.86
Median	1.97	1.76
Standard deviation	0.28	0.40
Range	1.6-3.2	1.43-3.14

P=0.035, paired *t*-test

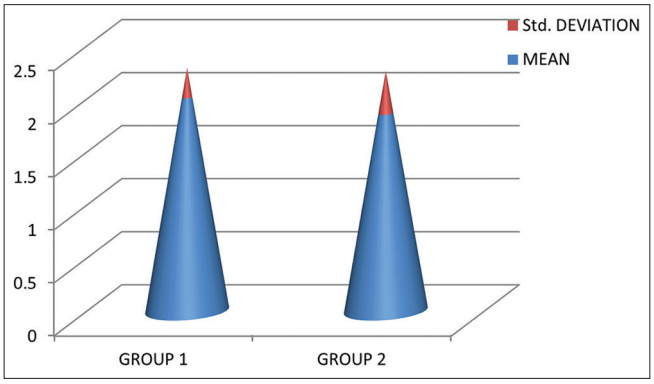


Table 6: Comparison of HbAlc levels in patients without retinopathy (Group 1) and patients with retinopathy (Group 2)

HbAlc	Group 1	Group 2
Mean	8.0	8.8
Median	8.11	8.45
Standard deviation	1.99	2.06
Range	5.6-13.1	6.2-12.2

P=0.011, paired *t*-test

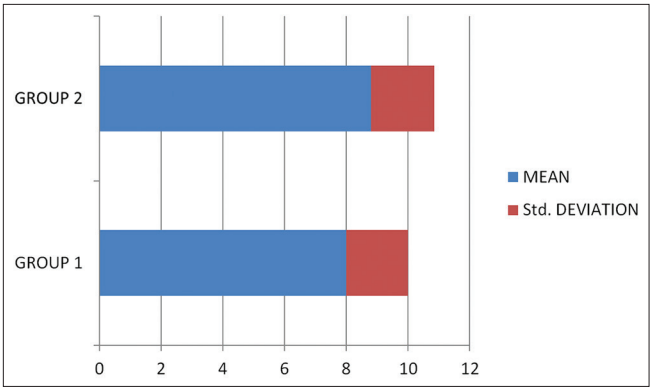
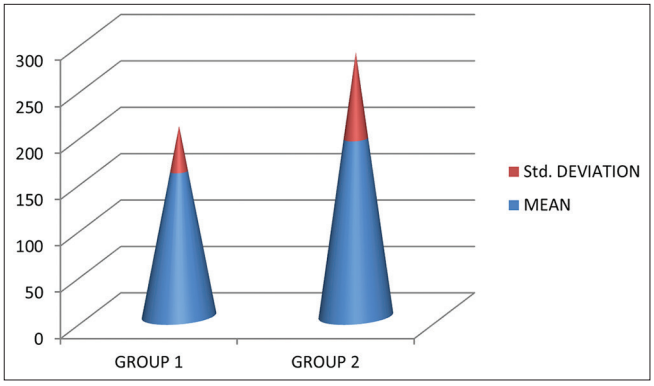


Table 7: Comparison of FBS levels in patients without retinopathy (Group 1) and patients with retinopathy (Group 2)

FBS	Group 1	Group 2
Mean	155.8	191.1
Median	149	167.5
Standard deviation	48.86	93.3
Range	74-304	79-498

P=0.020, paired *t*-test



DISCUSSION

Diabetes is becoming an emerging health problem in both developed and developing countries. The much-gained focus on the disease is due to the various complications that can occur secondary to diabetes. Diabetes itself increases the incidence of myocardial infarction and stroke and hence strict control is of utmost importance.[4]

Table 8: Comparison of PLBS levels in patients without retinopathy (Group 1) and patients with retinopathy (Group 2)

PLBS	Group 1	Group 2
Mean	217.7	253.1
Median	201	229.5
Standard deviation	72.1	135.5
Range	91 – 673	114 – 482

P=0.011, paired *t*-test

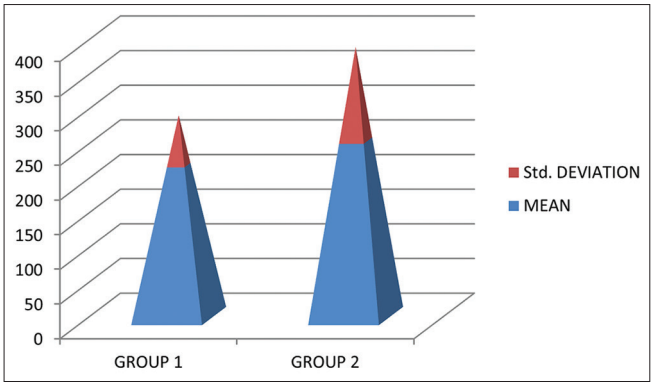
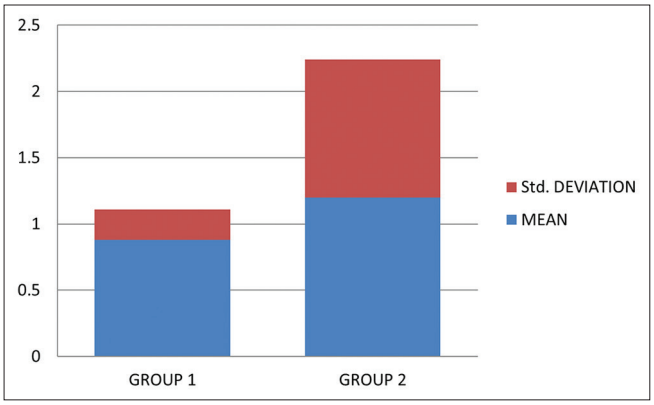


Table 9: Comparison of serum creatinine in patients without retinopathy (Group 1) and patients with retinopathy (Group 2)

Serum creatinine	Group 1	Group 2
Mean	0.88	1.2
Median	0.89	1.01
Standard deviation	0.23	1.04
Range	0.4-1.5	0.7-6.64

P=0.0086, paired *t*-test



Diabetic retinopathy is one of the most common microvascular complications of diabetes second to diabetic nephropathy. Diabetic retinopathy is also one of the leading causes of blindness in the developed world.[5]

Magnesium, its role in the progression of diabetes and its complications is not yet well established, but a number of studies show a lower level of magnesium in diabetic patients compared to their nondiabetic counterparts. Since use of magnesium is in multiple processes in the body, it is difficult to suggest that low magnesium levels itself lead to diabetes and its complications.[6]

Glycosylated hemoglobin which reflects the 3-month control of diabetes is also a strong predictor for diabetic retinopathy. A strict blood sugar control with HbAlc <7%, preprandial capillary plasma glucose between 70 and 130 mg% and postprandial capillary plasma glucose <180 mg% is recommended by ADA.

In our study, 100 patients of diabetes either attending the outpatients department or admitted hospital were included. A detailed history with special importance to family history and number of years of diabetes was taken. A complete clinical examination and required investigations as per the pro forma were done. The patients were divided into 2 groups on the basis of presence of diabetic retinopathy (Group 1) or the absence of diabetic retinopathy (Group 2).[7]

In the study out of the 100 patients, 46 are male and 54 are females. Group 1 consisted of 17 male and 33 female while Group 2 consisted of 29 male and 21 female patients. Most of the patients were in the age group of 51-70 years with 32 patients in Group 1 and 37 patients in Group 2. The mean age in Group 1 is 54.1 years and in Group 2 is 57.5 years.[8]

In our study, 41% patients had a history of diabetes up to 10 years with 26% and 23% patients with a history of 5 and 20 years of diabetes. Kahn *et al.* in their study of 965 patients at Joslin clinic showed a strong positive association between retinopathy and duration of diabetes of more than 10 years. A similar result was shown by Soto-Pedre *et al.* in their study. Wisconsin epidemiological study of diabetic retinopathy. 40% of the patients had a family history of diabetes while 60% did not have a family history.[9]

Serum magnesium levels in Groups 1 and 2 are compared. A mean value of 2.0 and standard deviation of 0.28 is seen in Group 1 while a mean of 1.86 with a standard deviation of 0.40 is seen in Group 2. The calculated $P = 0.035$ showed a significant correlation of serum magnesium with diabetic retinopathy. A low level of magnesium was seen in diabetic

Table 10: Correlation between serum magnesium and creatinine (within group)

Group	Correlation	Regression equation	R^2	*P*-value
Group 1	0.290	Serum magnesium = 1.70 + 0.355 creatinine	0.084 (no correlation)	0.041
Group 2	0.565	Magnesium = 1.57 + 0.223 creatinine	0.32 (no correlation)	0.001

retinopathy patients as compared to non-retinopathy diabetics. This is in sync with studies conducted by Hatwal *et al.* which showed similar results with a hypomagnesemia in diabetic retinopathy. Kareem *et al.* and Soto-Pedre *et al.* showed significant correlation between low serum magnesium and diabetic retinopathy.[9]

In our study, glycosylated hemoglobin levels are higher in Group 2 patients as compared to Group 1 with mean value of 8.8 in Group 2 and a mean value of 8 in Group 1. The $P = 0.011$ showed a significant correlation between glycosylated hemoglobin and diabetic retinopathy suggesting a strict blood sugar control to prevent the onset as well as the progression of diabetic retinopathy. The study was conducted by Klein *et al.* suggests a similar result with a consistent relationship between hyperglycemia and incidence and progression of diabetic retinopathy. Singh *et al.* also showed higher levels of glycosylated hemoglobin in diabetic retinopathy as compared to diabetics without retinopathy. However, their study did not show a significant correlation ($P = 0.6$) of glycosylated hemoglobin in proliferative diabetic retinopathy with background retinopathy. Raman *et al.* showed a glycosylated hemoglobin >8% was associated with sight-threatening diabetic retinopathy.[10]

The fasting blood sugar levels were higher in Group 2 as compared to Group 1. The $P = 0.020$ shows higher fasting sugar levels correlation with diabetic retinopathy (Group 2). Cheng *et al.*, in their study showed increase Wong *et al.* showed FBS >7 mmol/l having a sensitivity of only 40% for detecting diabetic retinopathy. However, the postprandial levels, in our study, in both the groups were similar with a $P = 0.11$, showing no significant correlation. This is against study conducted by Shiraiwai *et al.* who showed a significant correlation between postprandial sugar levels and progression of diabetic retinopathy.

The creatinine levels in the 2 groups showed a higher serum creatinine level in diabetic retinopathy patients (Group 2) as compared to non-retinopathy diabetics (Group 1). The $P = 0.0086$ was significant indicating the presence of renal involvement in diabetic retinopathy patients.[11]

Comparison within diabetic retinopathy patients showed a lower serum magnesium levels in proliferative diabetic retinopathy as compared to non-proliferative diabetic retinopathy patients. This is supported by evidence from studies by Hatwal *et al.* and Mcnair *et al.* who showed lower serum magnesium levels in the severest form of diabetic retinopathy as compared to background retinopathy.[12]

CONCLUSION

The final conclusion is that serum magnesium is low in patients in diabetic retinopathy and can be considered a risk factor for the development of the same in patients with diabetes. Correlation of magnesium should be considered, but long-term perspective trials will be required to prove the benefit.

Glycosylated hemoglobin levels correlate with the severity of diabetic retinopathy indicating strict control as hyperglycemia increases the risk for the development as well as the progression of the disease.

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Original Article

A Clinical Study on Reconstruction of Lip Defects

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Abstract

Introduction: Lips constitute the most important unit of the lower face having esthetic and functional roles, a delicate sensory apparatus, maintains oral competence, and determines facial expressions. Reconstructive lip surgery aims restore basic function, maintain sensation, and avoid cosmetic deformity.

Aim: To select a treatment protocol based on an algorithmic approach and evaluates the esthetic and functional outcomes of various surgical procedures for lip defects.

Materials and Methods: A total of 21 cases of lip defects resulting from various causes were studied. Their etiologies, reconstructive options, complications, and outcome in terms of functional and esthetics restoration were analyzed. An algorithmic approach to lip reconstructions was formulated and favored.

Results: Local flaps had excellent cosmetic and functional results, regional flaps gave satisfactory results, and distant flaps gave poor results.

Conclusion: For optimum results, use of local flaps and innervated myocutaneous flaps are advocated. Frozen section studies may help in ensuring adequate excisional margins and good long-term results.

Key words: Abbe Estlander flap, Esthetic units, Innervated myocutaneous flaps, Lip cancer, Lip switch, Nasolabial flaps, Perialar crescent excision, Vermilionectomy, Wide local excision

INTRODUCTION

Lip cancer and trauma are the two most common causes of lip defects. Other causes are infectious disease, vascular anomalies, clefts, vasculitis, and congenital nevi.[1]

Lip cancer is the most common oral malignancy (30%). Squamous cell carcinoma is the most common neoplasm of the lip. Basal cell carcinoma, melanoma, salivary gland carcinoma are others causes. Lower lip is the site of approximately 95% of all lip cancers with the upper lip only 5% of cases. Commissures are involved in <2% of cases.[2,3]

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Prolonged sun exposure (ultraviolet radiation) is the main cause. Factors of less significance are tobacco use, poor oral hygiene, alcoholism and syphilis.[4]

Male to female ratio 6:1 for all lip cancers. Most lip cancers are low grade and grow slowly with a propensity for lateral than vertical spread.[5]

Lymphatic drainage of upper lip and lateral part of lower lip is to the submandibular lymph nodes. The central third of lower lip drains to submental nodes. Cervical metastasis is seen in <8% of patients at the time of presentation. For and adequate cancer resection a 10 mm margin is generally preferred.

Traumatic lip injury occurs from human and dog bites and road traffic accidents (RTAs). The goal is to preserve all the lip tissue and reapproximate the wound edges with minimum tension.[6]

Critical land mark structures - White roll, philtral columns, mucosa - vermillion junction, and commissure are aligned

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first with key sutures. Muscle first, mucosa next, and skin last. When the defect includes more than 1/3 of the lip, primary closure is not possible. Local and regional flaps are used.

Aim

To evaluate the esthetic and functional outcomes of various surgical procedure for lip defect.

MATERIALS AND METHODS

Prospective observational study was conducted in the Department of the Plastic Reconstruction and Faciomaxillary Surgery, Madras Medical College. Institutional Ethics Committee approval and patients informed consent was obtained. Reconstruction of lip defects of various causes. Reconstruction of lip defects of various causes: Lip defects resulting from tumor ablation, traumatic lip defects, vascular anomalies, postcancrum oris defects were included in the study. Patients with tumor excision with involvement of margin, traumatic lip defects closed primarily were excluded.

Investigations

- Biopsy: Wedge biopsy from the edge of the growth
- Fine needle aspiration cytology (FNAC): Of the regional lymph nodes
- Computed tomography scan: To rule out bony involvement of mandible and maxilla
- Magnetic resonance imaging scan: To rule out infiltration of infraorbital or submental nerves.

Treatment

Pre-operative assessment

- Confirmation of complete tumor resection
- Recovery from associated injuries
- Optimum timing with respect to anesthetic risk
- Oral hygiene should be optimized.

Pre-operative planning

- Analysis of the defect
- Assessment of the available replacement tissue
- Design of the reconstruction.

General principles

- Motor and sensory innervation of each specific flap is preserved by careful dissection of the neurovascular pedicles
- The oral sphincter is reconstructed whenever possible
- Reconstruction is performed in esthetic units (Burget and Menick, 1985)[7]
- Meticulous attention to flap design as the cover and lining requirements may differ
- To select a treatment protocol based on an algorithmic approach to the problem for improving the outcome.

Procedures

In cancer patients

- Wide local excision (WLE) with 1.5 cm margins of clearance was done in 9 cases
  - Neck dissection was done in 5 cases
  - Supraomohyoid block dissection 2 cases
  - Suprahyoid block dissection 2 cases
  - Modified neck dissection in 1 case
  - Intraoperatively, tumor clearance was given priority with 1-1.5 cm margin. Reconstruction of the post excision defect was proceeded primarily.
- One patient underwent total vermilionectomy and reconstruction with V-Y musculomucosal advancement flap
- One patient, a post radiotherapy recurrent carcinoma of lower lip had wide spread disease involving floor of the mouth bases of the tongue and mandible and was referred to cancer chemotherapy unit
- One patient developed cardiorespiratory arrest during the surgery of WLE and neck dissection and succumbed later.

Upper lip reconstruction

- Bilateral inferiorly based nasolabial flap – 1 case
- WLE (partial thickness) and covered with split-thickness skin graft (SSG) – 1 case.

Lower lip reconstruction

- Reconstruction using inferiorly based nasolabial flap as unilateral Fujimori gate flap – 2 cases
- Reconstruction using cervical skin advancement – 1 case.

Commissure

- Right angle of mouth was reconstructed using a converse "Over and out" flap – 1 case
- Left angle of the mouth, both lips 15% and left cheek reconstructed with ipsilateral folded forehead flap – 1 case
- Left commissure and upper lip using a lower lip Abbe Estlander flap.

In trauma cases

- In defects <25% of total lip length wound debridement and primary repair was done in the acute setting. Wound debridement was kept to a minimum
- In defect >25% debridement and skin to mucosa approximation was done in the acute setting. Planned reconstruction was later done as a secondary procedure after the wound has settled well.
- Two lower lip defects were reconstructed with Estlander flaps from the lateral upper lip
- One case of upper lip defect was reconstructed using a lip switch flap from the lateral lower lip

- One case of blast injury of the lips and tongue was debrided and primarily repaired resulting in a central deficiency of both the lips and scarring. After recreating the defect, upper lip was reconstructed using bilateral perialar crescent excision and cheek advancement. The lower lip was reconstructed using the Schuchardt's principle
- One patient with post human bite nasal tip and columella and minor lip defect declined lip reconstruction and underwent nasal reconstruction
- One case of post human bite partial loss of lower lip dry vermillion underwent wound debridement and SSG
- Another case of post human bite central upper lip defect underwent wound debridement and skin to mucosa approximation awaits secondary reconstruction (Table 1).

Low Flow Vascular Anomalies

Low flow vascular anomalies were subjected to pre-operative sclerotherapy using intralesional injection of 1% sodium tetradecyl sulfate 3-4 doses in 3 weeks intervals. After sufficient fibrosis, lesions were excised and primary repair done.

Infectious Diseases

One case of polycystic ovarian disease central upper lip defect was reconstructed using a central Abbe flap from lower lip.

Choice of suture material

For a three-layered closure mucosa is closed with chronic suture, muscle with vicryl/polydioxanone suture and skin with monofilament nylon/prolene.

Post-operative care

- Frequent use of mouthwash
- Application of antibiotic ointment/petroleum jelly with nonadherent light absorptive dressings
- Early liquid diet followed by semisolid diet.

Follow-up

- At appropriate intervals for return of function
- Physical therapy for avoiding scar contracture
- Detection of early recurrences following tumor ablation.

Tests to perform

- Oral competence: Assessed by water holding test[8]
- Oral aperture: Normal interincisal distance measurement ≥40 mm
- Assessment of cosmetic outcome.

RESULTS

All patients were followed up for tumor control, improvement in appearance, oral competence, speech and animation. In 21 cases, 15 are male patients and 6 are female, mean age 49.8 years. Patients with following complaints; tumor related - 9 cases, cosmetic deformity - 21 cases, drooling - 7 cases, speech difficulty - 12 cases. Causes are followed; postsurgical - 13 cases (tumor ablation and vascular anomalies), posttraumatic - 7 cases, postinfective - 1 case. Site: Upper lip - 9 cases, lower lip - 11 cases, and commissures - 11 cases. Percentage of tissue loss and thickness varied from minor to near total loss of the lip. Most of the patients have full thickness loss of the lip. Tumor ablation patients: Squamous cell carcinoma - 9 cases, dysplasia - 1 case, malignant adnexal tumor - 1 case. Well differentiated squamous cell carcinoma was the most common histopathological variant (5 cases) followed by verrucous squamous cell carcinoma (2 cases) and high grade malignant squamous cell carcinoma (2 cases). 2 patients were post radiotherapy residual/recurrent squamous cell carcinoma (Figures 1-6).

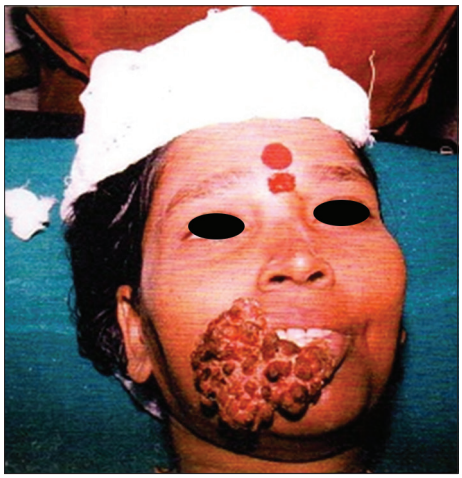

Figure 1: Squamous cell carcinoma lower lip and right commissure

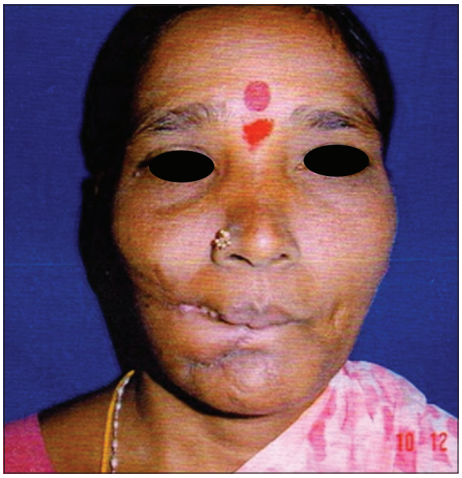

Figure 2: Squamous cell carcinoma lower lip and right commissure postsurgery

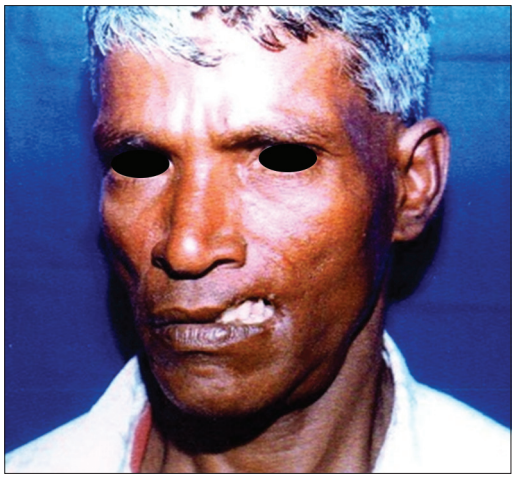

Figure 3: Post human bite upper lip defect

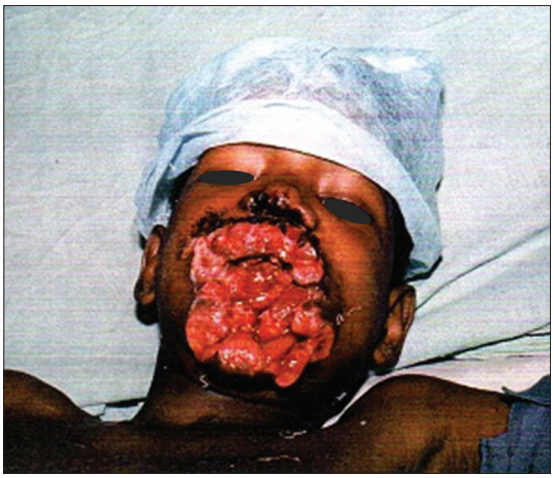

Figure 5: Blast injury: Shattered lips and tongue

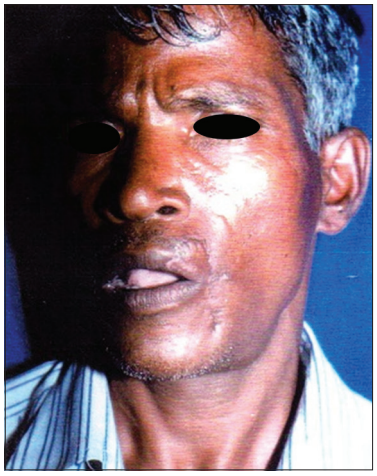

Figure 4: Post human bite upper lip defect postsurgery

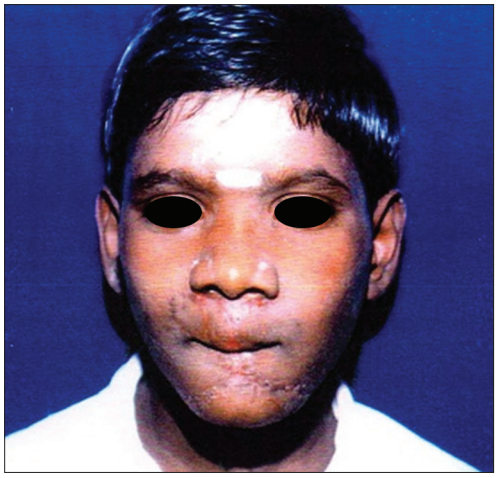

Figure 6: Blast injury: Shattered lips and tongue postsurgery

Tumor Status

Most cancers were clinically advanced.

- T4: 5 cases
- T3: 2 cases
- T2: 3 cases
- Dysplasia: 1 case.

The Nodal Status

- Ipsilateral submandibular lymph nodes: 8 cases
- Submental lymph nodes: 2 cases
- Upper deep cervical: 1 case
- Contra lateral nodes: 2 cases.

None of the patients had detectable metastasis at the time of the presentation.

Trauma Cases

- Post human bite: 4 cases
- RTA: 2 cases
- Blast injury: 1 case.

Vascular Anomalies

- Low flow arteriovenous malformation: 1 case
- Venous malformation: 1 case.

Infections

Postcancrum oris defect: 1 case.

Patients underwent regular clinical workup, routine laboratory investigation, and specific investigations. All cancer patients underwent biopsy confirmation of the tumor, FNAC of the enlarged lymph nodes and radiological investigations to rule metastatic spread. Traumatic lip defect cases were evaluated for associated faciomaxillary injuries. All patients were subjected to treatment planning for delineating the defect and arriving at the most appropriate procedures for the given lip defect. Preoperatively, patient is informed about the risk, alternatives and various stages involved and consent obtained. Oral hygiene was optimized preoperatively. Patients were taken up under general anesthesia under prophylactic antibiotic cover.

Local Control

- After WLEs 4 cases had excisional margins positive for tumor cells. All cases were referred for post-operative radiotherapy
- One patient developed local recurrence in the post-operative period underwent local excision and post-operative radiotherapy.

Regional Control

- All cases were free from residual or recurrent disease in the neck nodes.

Cosmetic Results

- Local flap like lip switch had excellent cosmetic results
- Regional flaps such as nasolabial flaps and check advancement flaps gave satisfactory results
- Distant flaps like forehead flaps gave poor results.

Functional Outcome

- Oral competence and speech were preserved in the local and regional flaps
- Distant flaps had poor functional outcomes
- There was subjective improvement in all cases and the patients were satisfied
- Overall functional outcomes were comparable with cosmetic results.

Complications

Mortality

One case of carcinoma right cheek and lips T4 N2b Mo, following excision and supraomohyoid block dissection succumbed in the post-operative period due to cardiorespiratory arrest (Table 2).

Table 1: Distribution surgical procedures

Procedures	Cases
WLEs	9
Neck lymph node dissections	5
Lip switch, Estlander flaps	4
Fujimori gate flaps	2
Bilateral inferiorly based nasolabial flaps for upper lip	1
Converse "over and out" flap for commissure	1
Folded forehead flap	1
Cervical skin advancement flap for lower lip	1
Bilateral perialar crescent excisions and cheek advancement	1
Schuchardt's principle flap	1
Central Abbe flap	1
SSG	2
Sclerotherapy and local excision of vascular lesions	2

SSG: Split-thickness skin graft, WLE: Wide local excision

Table 2: Distribution of complications

Oral incompetence	2 cases
Hypoesthesia with mild drooling	4 cases
Microstomia	1 case
Local recurrence	1 case
Partial wound dehiscence	1 case
Distortion of features	1 case

DISCUSSION

An algorithmic approach to lip reconstruction is favored. The major goals of reconstructions are Oral competence, adequate oral aperture and motion, normal anatomic proportions. Adherence to basic principles gives letter results. As a complex reconstructive procedure price to establishment of adequate margins can certainly compromise the ultimate result, it is appropriate not to perform closure until margins have been adequately examined. Functional reconstructions are best accomplished with innervated myocutaneous flaps of orbicularis oris for both lips[9] or the depressor anguli oris lower lip or the innervated levator anguli oris flap[10] for upper lip. Upper lip reconstructions are more challenging because of the presence of central lip structures and hair bearing skin in the males. As lower lip is more important for oral competence, local with intact innervations is preferable.

CONCLUSION

For optimum result, use of local flaps and innervated myocutaneous flaps is advocated. Use of other tissues/flaps result in esthetic and functional compromise. Frozen section studies may help in ensuring adequate excisional margins and good long-term results. In trauma, after debridement, primary reconstruction can be done if crush injuries, traumatized vascular pedicle or other life – threatening injuries can be excluded.

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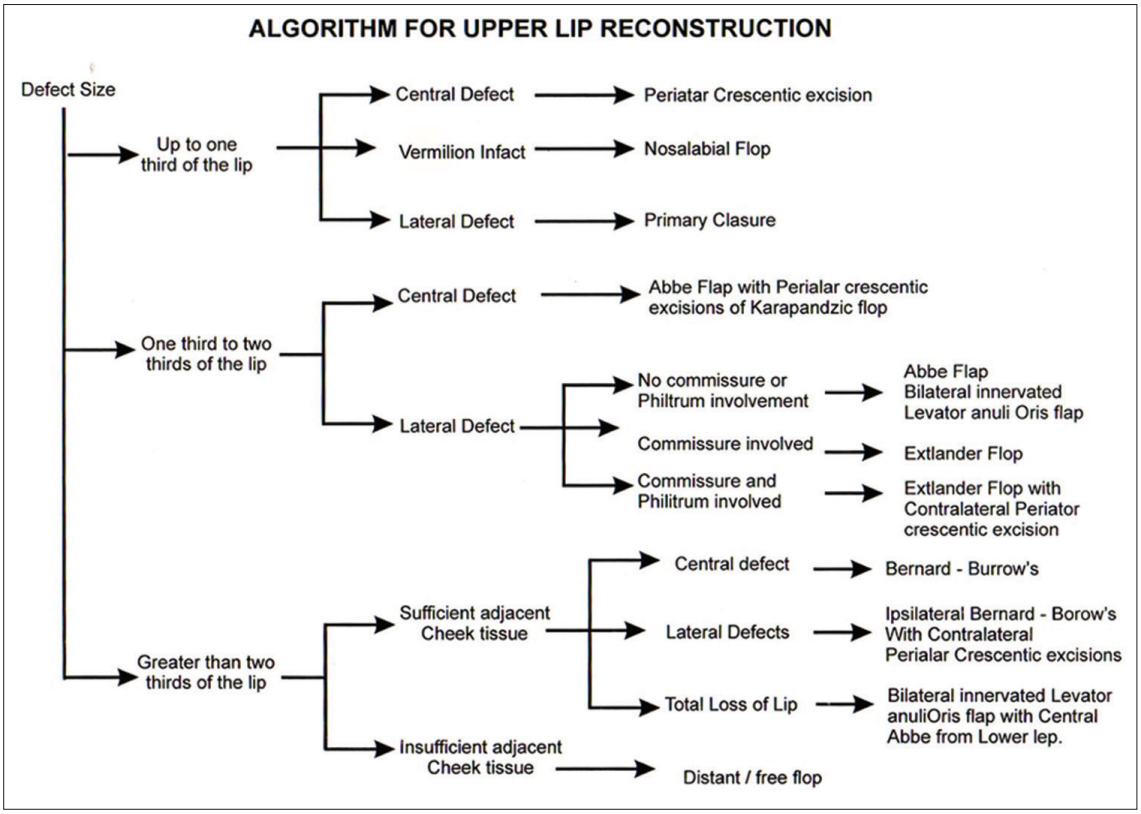
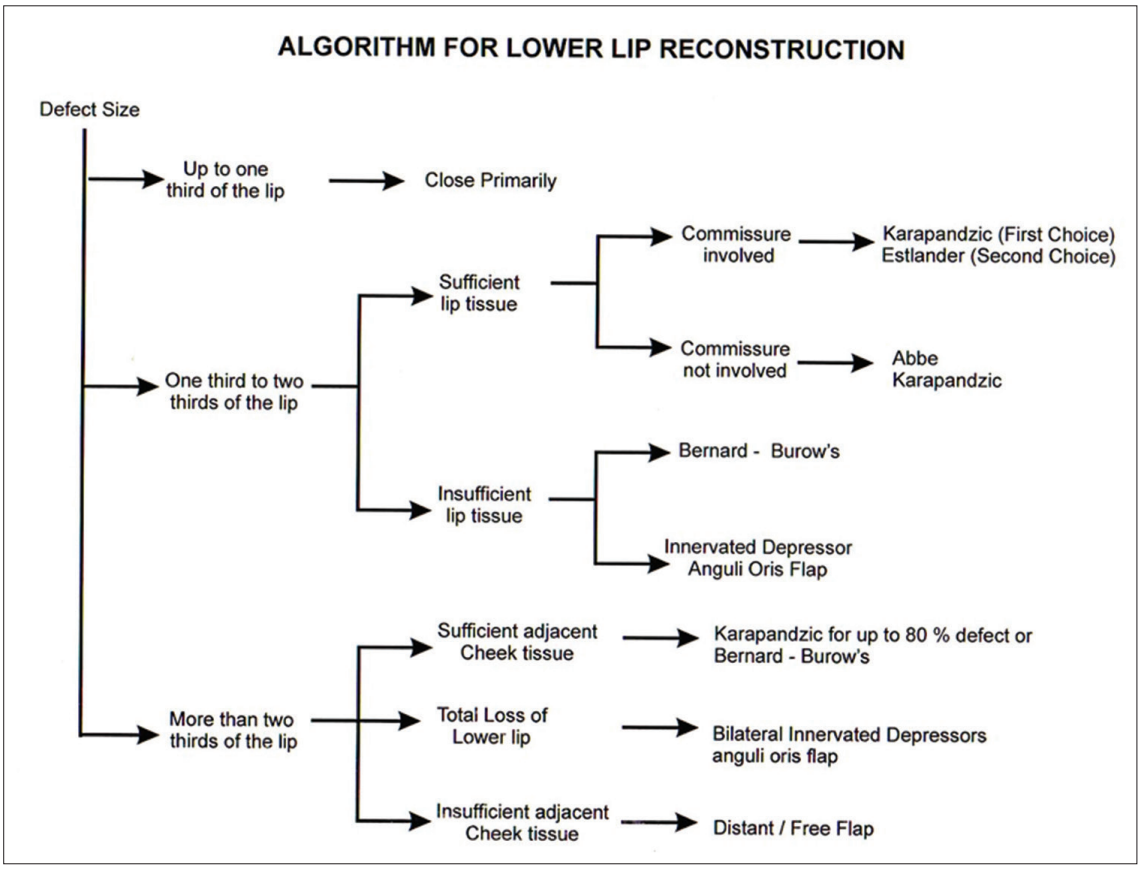
ALGORITHMS


ALGORITHM FOR UPPER LIP RECONSTRUCTION
Defect Size
Up to one third of the lip
Central Defect
Periatar Crescentic excision
Vermilion Infact
Nosalabial Flop
Lateral Defect
Primary Clasure
One third to two thirds of the lip
Central Defect
Abbe Flap with Perialar crescentic excisions of Karapandzic flop
Lateral Defect
No commissure or Philtrum involvement
Abbe Flap Bilateral innervated Levator anuli Oris flap
Commissure involved
Extlander Flop
Commissure and Philitrum involved
Extlander Flop with Contralateral Periator crescentic excision
Greater than two thirds of the lip
Sufficient adjacent Cheek tissue
Central defect
Bernard - Burrow's
Lateral Defects
Ipsilateral Bernard - Borow's With Contralateral Perialar Crescentic excisions
Total Loss of Lip
Bilateral innervated Levator anuliOris flap with Central Abbe from Lower lep.
Insufficient adjacent Cheek tissue
Distant / free flop


ALGORITHM FOR LOWER LIP RECONSTRUCTION
Defect Size
Up to one third of the lip
Close Primarily
One third to two thirds of the lip
Sufficient lip tissue
Commissure involved
Karapandzic (First Choice) Estlander (Second Choice)
Commissure not involved
Abbe Karapandzic
Insufficient lip tissue
Bernard - Burow's
Innervated Depressor Anguli Oris Flap
More than two thirds of the lip
Sufficient adjacent Cheek tissue
Karapandzic for up to 80 % defect or Bernard - Burow's
Total Loss of Lower lip
Bilateral Innervated Depressors anguli oris flap
Insufficient adjacent Cheek tissue
Distant / Free Flap

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Original Article

Effect of Triclosan Containing Tooth Paste and Conventional Fluoride Tooth Paste on Plaque and Gingivitis: A Randomized Clinical Trial

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Abstract

Background: Oral hygiene is the important component of personal hygiene. Tooth brushing is the most common and effective method of oral hygiene practice among all methods. To improve the efficacy and effectiveness of tooth brushing certain chemicals such as triclosan and fluoride are being incorporated into the dentifrices.

Aim: This study was aim to assess the effect of triclosan containing tooth paste and conventional fluoride tooth paste on plaque and gingivitis.

Materials and Methods: 12-year-old schoolchildren were involved in the study. A total of 56 children were randomly divided into two groups, Group 1 (28 children): Triclosan containing tooth paste and Group 2 (28 children): Fluoride containing tooth paste. Clinical examination was carried out using Silness and Loe plaque index (PI) and Loe and Silness gingival index (GI). Independent *t*-test and paired *t*-test was used for the intergroup and the intragroup comparison.

Results: There were totally 56 children included, 34 (60.7%) boys and 22 (39.3%) girls. Moreover, there was a statistically significant difference was found between the Group 1 and Group 2 after intervention ($P < 0.001$) with respect to the PI and GI. There was also a statistically significant difference between the baseline and after intervention score in Group 1 ($P < 0.001$) with respect to the PI and GI.

Conclusion: This study concluded that triclosan containing tooth paste has shown better in reduction of plaque scores when compared to the conventional fluoride containing tooth paste.

Key words: Dental plaque, Fluoride, Gingivitis, Tooth paste, Triclosan

INTRODUCTION

Dental caries and periodontal diseases, the two arch criminals of the oral cavity, are essentially caused by the microorganisms present in the dental plaque.[1] The use of toothpaste has ancient roots. Ancient Greeks, Egyptians, and Roman civilization were known to develop their own tooth "powder" containing pumice, talcum, coral powder. W.D. Miller ushered a new era in the science of preventive dentistry in 1890 when he described his chemicoparasitic theory of tooth decay. This new theory created a boom in the toothpaste industries with each manufacturer adding special agent/agents. The more modern aspect of dentifrice came after the Second World War and with greater understanding about the pathogenesis of periodontal disease.[2]

Dental plaque is a microbial biofilm which is invariably present on the hard and soft tissues of oral cavity and it contains a complex blend of various microorganisms. It is considered as the precursor of dental caries, gingivitis, and periodontitis. The prevention and control of dental caries and as well the periodontal disease is dependent on optimal plaque control.[3]

The role of plaque accumulated at the gingival margin in the initiation and progression of gingivitis and periodontitis has been well documented.[3] The mechanical

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removal of such deposits on a regular basis is one of the principal methods advocated by the researchers and clinicians. However, mechanical plaque removal is not always performed to an adequate standard as many surfaces on the teeth and gingiva are relatively inaccessible for mechanical cleansing and added to this fact, it also depends on the manual dexterity of the performer. As a result, chemotherapeutics have been introduced as adjunct to mechanical removal of plaque. The supplementation of mechanical brushing with effective adjunctive chemotherapeutic agent was found to have a beneficial effect on gingival health as the chemicals used could prevent the growth of dental plaque on human teeth.[4]

The triclosan molecule in dentifrices seems to possess several properties: Plaque-reducing and antigingivitis effects are documented which are based on antibacterial action combined with the potential of triclosan to influence several mediators of inflammation. No side effects are described in the corresponding literature.[5] Fluoride is another antimicrobial agent in addition to its anticariogenic effect, which has been incorporated in tooth pastes and mouth rinses since long time to prevent the plaque accumulation on the tooth surface. Hence, this study was aim to assess the effect of triclosan containing tooth paste and conventional fluoride tooth paste on plaque and gingivitis.

MATERIALS AND METHODS

Ethical approval was obtained from the Institutional Review Board SJM Dental College and Hospital, Chitradurga, and informed consent was obtained from all the parents/guardians before the study conducted. This study comprised 12-year-old schoolchildren.

Children who were regular users of toothbrush and toothpaste for maintaining oral hygiene and willing to participate were included in the study. Students with known systemic illness, recent antibiotic and anti-inflammatory therapy, history of allergy to toothpaste, who were undergoing orthodontic treatment and who wore prosthodontic appliances were excluded from the study.

56 children were divided into two groups:

- Group 1 (28 children): Triclosan containing tooth paste
- Group 2 (28 children): Fluoride containing tooth paste.

Initially, all the subjects in both the groups underwent a wash out period of 2½ days to rule out any possible carry over effects of the previously used oral hygiene products. The wash out was done by brushing with water alone and then followed by a treatment period of 30-day. Baseline clinical examination was carried out to assess plaque using Silness and Loe plaque index (PI) and gingivitis by Loe and Silness gingival index (GI) by a single trained, calibrated examiner. After recording, the indices participants were subjected to prophylaxis to render them plaque, stain, and calculus free. Following the prophylaxis, the study participants were randomly allocated into Group 1 triclosan containing tooth paste and Group 2 fluoride containing tooth paste.

The tubes containing the dentifrices were previously packed similarly and coded to warrant that neither the examiner nor the volunteers knew their content. The participants were given similar type of toothbrush and taught tooth brushing technique for the purpose of standardization. Furthermore, participants were instructed to brush twice daily (morning immediately after waking up and night before going to bed) for 2 min using the toothbrush and toothpaste given to them.

Randomization, allocation concealment, and distribution of the toothpaste were done by the coresearcher who was not involved in the clinical examination. The subjects were recalled for clinical examination after 30 days. The coresearcher revealed the content of each tube only after completion of the study.

Statistical Analysis

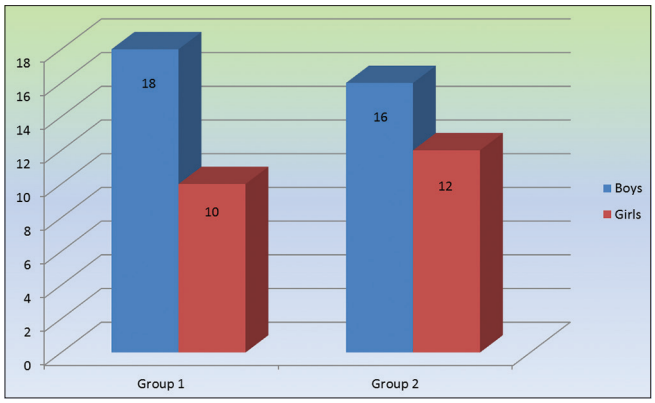
SPSS version 20 was used to analyze the data. Descriptive analysis has been done, and data were analyzed using independent *t*-test and paired *t*-test. The level of significance was set at 5%.

RESULTS

Graph 1 shows that there were totally 56 children included 34 (60.7%) boys and 22 (39.3%) girls. In that 18, 16 boys and 10, 12 girls were randomly allotted to Group 1 and Group 2, respectively.

Table 1 shows that there was a statistically significant difference was found between the Group 1 and Group 2 after intervention ($P < 0.001$) with respect to the PI. There was also a statistically significant difference between the baseline and after intervention score in Group 1 ($P < 0.001$) with respect to the PI.

Table 2 reveals that there was a statistically significant difference was found between the Group 1 and Group 2 after intervention ($P < 0.001$**)** with respect to the GI. There was also a statistically significant difference between the baseline and after intervention score in Group 1 ($P < 0.001$**)** with respect to the GI.



Graph 1: Distribution of gender

Table 1: Intra and inter group comparisons of PI at baseline and after intervention

Variables	Group 1	Group 2	*P* value
Baseline			
N	28	28	0.124
Mean±SD	0.86±0.16	0.78±0.18	
After intervention			
N	28	28	0.001*
Mean±SD	0.46±0.20	0.70±0.19	
t-value	6.41	4.37	
P value	0.001*	0.142	

*Significant. SD: Standard deviation, PI: Plaque index

Table 2: Intra and Inter group comparisons of GI at baseline and after intervention

Variables	Group 1	Group 2	*P* value
Baseline			
N	28	28	0.530
Mean±SD	0.44±0.12	0.43±0.18	
After intervention			
N	28	28	0.001*
Mean±SD	0.36±0.10	0.42±0.14	
t-value	3.10	2.40	
P value	0.001*	0.06	

*Significant. SD: Standard deviation, GI: Gingival index

DISCUSSION

A majority of oral diseases exhibit multifactorial etiology. The interplay of host, agent and environmental factors ultimately determine the oral health status of an individual. Dental caries and periodontal disease are two major and most common oral diseases which show widespread distribution among different populations in the world.

Dental caries is the most prevalent chronic disease affecting the human race when unchecked in its incipient stage it destroys the tooth structure leaving an indelible mark on tooth form and structure. Periodontal disease is the generic name given for a group of diseases which affect the periodontal apparatus, and initially it appears as simple gingivitis, if not checked it may extend to deeper tissues resulting in periodontal destruction leading to tooth loss. Dental plaque is considered to be the precursor for both dental caries and periodontal disease. The complex microbial ecosystem of dental plaque along with the metabolic byproducts poses a profound challenge on the integrity of hard and soft tissues of the oral cavity.

This study shows statistically significant difference between the baseline and after intervention score in Group 1 ($P < 0.001$) with respect to the PI and GI. Similar results were obtained in other studies published in the literature such as Lindhe *et al.*,[7] Rosling *et al.*,[8] Cullinan *et al.*[9] This may be attributed to the triclosan present in the dentifrice which is a potent antiplaque agent. The studies of Ramberg *et al.*[10] have confirmed the potent antiplaque effect of triclosan. Since triclosan has plaque inhibitory property, obviously it reduces the gingival inflammation. Moreover, triclosan acts on the cyclooxygenase and lipooxygenase pathways of inflammation and inhibits the inflammatory mediators. The parallel reduction in gingival scores may be attributed to dual role of triclosan as a potent antiplaque agent and also anti-inflammatory agent.[11]

In this study, there was no intra and inter group significant difference was found in the Group 2 with respect to the PI and GI. There are other studies in conformity with this result.[11,12] These studies have also shown that there are significant reduction in the plaque scores at the end of the study when compared to the baseline. This result shows that the fluoride containing dentifrice has antiplaque activity. Fluoride alone also acts as a bacteriostatic in lower concentrations by affecting the metabolism of the bacteria.

The strength of the study was its randomized controlled design. The limitation of the study is its small sample size. In future, such a study has to be designed with larger sample size to further validate this study results. Besides, experimental period of 30-day may not be sufficient to show conclusive evidence of superiority of the test toothpaste over the control dentifrice.

CONCLUSION

Within the limitation, this study concluded that triclosan containing tooth paste has shown better in reduction of plaque scores when compared to the conventional fluoride containing tooth paste.

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Original Article

Age-specific Bone Mineral Density Values from Multi-skeletal Sites in Normal Indian Female Population

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Abstract

Background: Data on age-specific normal bone mineral density (BMD) values for the Indian population are scarce. This study aims to find out the normal values of BMD in an all-female urban population. Since BMD and its derivatives are used widely for identifying early osteopenia in the elderly age group, data on normal subjects have both clinical and research utility. We also examined the relationship between body mass index and BMD.

Materials and Methods: We studied the bone mineral densities of 500 asymptomatic Indian females across five age groups (100 in each age group) and analyzed the data for mean values and for percentage decrease every 10 years. The bone mineral densities were measured through a dual energy X-ray absorptiometry (DEXA) on the Hologic QDR densitometer. The patient enrolment was on a voluntary basis. Volunteers with conditions which may affect the BMD value (very low body weight, high-risk medication use, and chronic kidney disease or other conditions associated with bone loss) were excluded from the analysis. The mean values were then compared with western data to assess if the BMD were comparable.

Results: Mean hip BMD for age group 30-39 years was 1.199; for the 40-49 years age group was found to be 0.939; for the 50-59 years age group was 0.848; in the 60-69 years mean BMD was 0.842; and 0.718 was the mean BMD in the 70-79 years age group. An average fall of 11% every 10 years was found with the sharpest dip between ages 30 and 50.

Conclusion: Bone mineral densities decline by an average of 11% every 10 years in females. Normal values for age-matched Indian females were comparable with western data. Our sample size was sufficient enough to extrapolate the mean age-matched values to the entire population.

Key words: Bone mineral density, Dual energy X-ray absorptiometry scan, Osteopenia

INTRODUCTION

The rise in the incidence of osteoporosis in the world prompted various diagnostic procedures to assess bone density.[1,2] Several noninvasive techniques are available for estimating bone density, such as single energy X-ray absorptiometry, dual energy X-ray absorptiometry (DEXA), quantitative computed tomography, genetic testing,[3] and ultrasound.[4,5] Of these, DEXA is widely used in modern practice and utilizes two X-ray energies to estimate the area of the mineralized tissue, and the mineral content is divided by the area. The bone mineral density (BMD) values so obtained are compared to that of a normal population (thereby computing the T-score) and with people of the same age, thereby computing the Z score. A Z score of >−1 or T score >−2.5 (i.e., more than 2.5 standard deviations [SDs]) in the hip or femoral neck is the definition of osteoporosis.[6,7] Each SD increase in T score in adults in associated with 1.5-3-fold increase in fracture risk.[8,9] These scores are generally calculated in multi-skeletal sites, namely the hip, spine, and radius. The World Health Organization criteria for the diagnosis osteoporosis are summarized in Table 1.

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Table 1: Analysis of variance of hip, spine, and radius BMD

Parameter	Sum of squares	df	Mean square	F	Significant
Hip BMD					
Between groups	12.894	4	3.224	170.875	0.000
Within groups	9.338	495	0.019		
Total	22.333	499			
Spine BMD					
Between groups	5.412	4	1.353	118.022	0.000
Within groups	5.675	495	0.011		
Total	11.087	499			
Radius BMD					
Between groups	0.907	4	0.227	23.336	0.000
Within groups	4.811	495	0.010		
Total	5.718	499			

The DEXA has become the standard for assessing the longitudinal BMD in clinical practice and for pharmaceutical trials after Hologic Inc. introduced it in 1987.[6,10] After John Cameron proposed the idea of measuring bone mass more than 60 years, the concept, application, technology, and interpretation of DEXA has undergone a revolution, forever cementing its place in modern medicine.[11,12]

The basic principle behind DEXA is low and high energy photons through the body which assumes that the body is made of two compartments, the bone mineral and soft tissue with varying attenuation coefficients.[13] The ease of availability of this technology, the drastic reductions in scan times to as less as 3 min and the overall curiosity among the general population to know their "bone strength" has led to widespread and rampant use of "DEXA" in recent times. A lot of data have been generated which the avid clinician must know is dependent on various factors. Gender and age specific variations, equipment manufacturer specific differences, and disease processes can all affect the values obtained after a regular scan.

DEXA is not without its limitations. It provides two-dimensional interpretation for a three-dimensional bone structure.[5] Therefore, its measurements are expressed in g/cm^2 rather than a volumetric expression like g/cm^3. Bone thickness is not factored into the equation, which may cause some confounding in the values obtained.[14] Many authors recommend BMD be suitably modified to involve body size to achieve a more realistic estimate.[15,16] Projection artefacts (distance of scanned area from the beam source, changes in surrounding soft tissue causing altered read and thin bones children) can also alter values and their interpretation.

The main shortcoming of such a modality, which is being used with increasing frequency in the Indian urban setting, is a lack of normative data for the Indian population. The definition for "normal" has far reaching implications on diagnosis, treatment, and prognosis in a variety of disorders. A falsely low BMD might subject the Indian patient to unnecessary tests and interventions. Conversely, a "normal" BMD may deprive the patient of medications which may benefit his disease process. Recently, body mass index is being taken into cognizance for greater accuracy of required results. DEXA is being routinely used for assessing fracture risk in patients with both primary and secondary osteoporosis.[17,18] For fracture risk, specifically, newer scores have been developed, such as the FRAX, Garvan score, and the Q fracture score.[4,19,20] Furthermore, DEXA is finding application structural analysis of joints and visceral fat analysis as well.[10]

Aims and Objectives

To study of the age-specific BMD values from multi-skeletal sites in normal asymptomatic Indian female population.

MATERIALS AND METHODS

We conducted a single center, observational study where patients were recruited from the out-patient department to undergo DEXA on a volunteer basis. We tried to ensure adequate representativeness from the participants, i.e., diverse weight, height, and ethnic backgrounds. Written consent was obtained. Detailed medical, surgical, and drug history were obtained. Participants meeting any exclusion criteria (see below) were excluded from the study. A total of 500 participants entered the study. The participants underwent a multi-skeletal site (total hip, lumbar spine, and left radius, both 33% and ultradistal) DEXA scan using a Hologic QDR densitometer after a detailed anthropometric analysis. The operator for all scan was the same to ensure uniformity in the protocol. The data were collected over a period of 15-month March 2015 to June 2016.

Inclusion Criteria

The study included asymptomatic female patients who were selected after a baseline evaluation which included complete hemogram, liver and renal function tests, sugars, and thyroid profile.

Exclusion Criteria

Our endeavor was to exclude participants with conditions predisposing to early bone loss. These include (1) Diabetes, both Type 1 and Type 2,[21] (2) early menopause, (3) steroid use (>7.5 mg of prednisolone or equivalent) for >3 months, (4) previous cancer chemotherapy including, but not limited to aromatase inhibitors, (5) low body weight (BMI <17 kg/m^2), (6) hyperthyroidism or hypothyroidism, (7) malabsorption disorders, (8) major depression or

antipsychotic medication intake, (9) chronic kidney disease,[22] (10) monoclonal gammopathies, (11) organ or marrow transplant, and (12) hypogonadism. The patients were meticulously screened for any conditions which may alter the average for the representative population.

Statistical Analysis

We calculated the T scores (labeled osteopenia as T-score between −1 and −2.5, and osteoporosis >−2.5) for the study population using the peak BMD and SD levels and found a prevalence of osteopenia of 36% ($P < 0.001$) in the 60-69 age group population and 41% ($P < 0.001$) in the 70-79 years age group. However, our study was neither powered nor intended to assess the prevalence of osteopenia. To test whether BMI, hip BMD, spine BMD, and radius BMD differ significantly across the age groups, the statistical tool "one-way ANOVA" is used. All the assumptions of one-way ANOVA are tested and satisfied for normality by the data set collected before applying one-way ANOVA. The statistical analysis is shown in Table 1. The variation of BMD with age is shown in Bar Diagram 1.

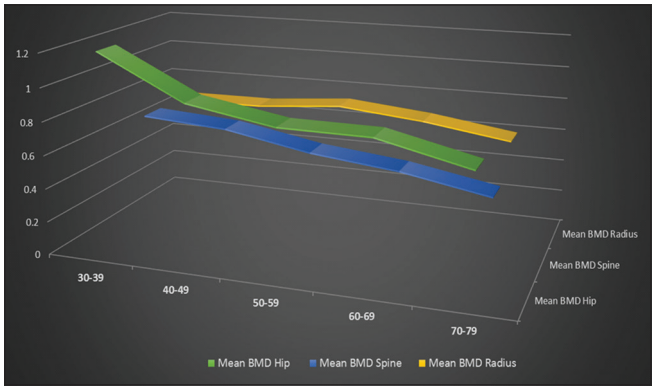
Hip BMD

The *post hoc* tests suggest that the mean hip BMD scores are nearly same for age groups "50-59 years" and "60-69 years." The hip BMD is decreasing as the age increases.

The age group with the highest hip BMD is "30-39 years;" then it is "40 -49 years;" then it is for "50-59 years" and "60-69 years." It is least for age group "70-79 years."

Spine BMD

The *post hoc* tests suggest that the mean spine BMD scores are nearly same for age groups "30-39 years" and "40-49 years," The spine BMD is decreasing as the age increases. The age group with the highest spine BMD is "30-39 years" and "40-49 years"; then it is for "50-59 years"; then "60-69 years." It is least for age group "70-79 years."



Bar Diagram 1: Variation of bone mineral density with age

Radius BMD

The *post hoc* tests suggest that the mean radius BMD scores are nearly same for age groups "30-39 years," "40-49 years" and "60-69 years." The age group with the highest radius BMD is "50-59 years;" then it is for "30-39 years" and "40-49 years" and "60-69 years." It is least for age group "70-79 years."

RESULTS

Hip

Peak BMD was in the 30-39 years' ($n = 100$) age group with a mean BMD of 1.199 g/cm^2. In next group of 40-49 years ($n = 100$), the mean BMD was 0.939 g/cm^2. For the next two groups of 50-59 years ($n = 100$) and 60-69 years, the mean BMD was 0.848 g/cm^2 and 0.842 g/cm^2 Predictably, the lowest BMD was in the 70-79 years' age group with a mean of 0.718 g/cm^2. The greatest loss of BMD was between ages of 30 and 50 years. The average loss every 10 years was 11%.

Spine

In the 30-40 years, the mean BMD was 0.692 g/cm^2. In the next 3 groups of 40-49 years, 50-59 years, 60-69 years the mean BMD was 0.656 g/cm^2, 0.559 g/cm^2, and 0.501 g/cm^2. In the 70-79 years group, the mean BMD was 0.404 g/cm^2.

Radius

The mean BMD for the various age groups was found to be 0.789, 0.699, 0.699, 0.599, and 0.511, respectively. The average in bone density is reduced by 10% every 10 years. The variance of BMD in hip, spine, and radius is shown in Table 1.

DISCUSSION

Bone densitometry has become the gold standard in the diagnosis and evaluation of osteoporosis. A second DEXA is often to assess therapeutic response. As the obesity, epidemic rages on in the Indian subcontinent, osteoporosis prevalence are sky high, with some estimates ranging from 45% to 50% in elderly patients. DEXA is also being with increasing frequency for patients on long-term corticosteroid therapy, which in itself has a wide range of indications in modern clinical practice today. In 2008, Makker *et al.* established in a landmark study,[23] the normative values for bone density in Indian subjects. They also observed that BMD for Hip in women was lowest in the Ward's triangle (the inferomedial end of the neck of femur). However, Ward's triangle is rarely ever selected in clinical practice for evaluation or diagnosis due to stark variations on densitometry. Our results compare well this

study. However, in their study, the established that peak BMD for the radius ultradistal was achieved at the 20-29 years in females, a group which was not part of our study. Hence, our findings still show the age group 30-39 years to have peak values at all skeletal sites, including the radius. Furthermore, a significantly lower fraction (36% in 60-69 years' group and 41% in the 70-79 years' group) of our "normal" participants had osteopenia or osteoporosis. Furthermore, our data suggests a 9-11% reduction in BMD every decade. Our figures are, however, commensurate with the national average prevalence for osteoporosis.

We were unable to demonstrate a change (more specifically, a fall) in BMD in the groups which represent transitions between pre- and post-menopausal women. These groups, namely, ages ranging from 40 to 49 years were expected to depict intra-group variation in BMD, seemingly due to the fraction of participants who were either peri- or post-menopausal. We did not observe any increase in BMD after the age of 70 as reported in some series. Overall, as the graph shows, BMD varied inversely with age. It is unclear whether volumetric BMD in g/cm^3 can be extrapolated or even compared to this data. Further studies with bone mineral apparent density are required.

We set out to investigate normal values of bone density. True to the research question, we eliminated participants aged >80 years. While fully aware that bone density would vary the most in this group, we identified that it would contribute little to our quest for the normal. Our study does not include data from the 20 to 29 age group as well, which was in part due to the paucity of this age group undergoing bone densitometry. The absence of this particular group was acceptable to our investigators since all data presented herein is age specific and not absolute. Our study participants included only women as this was a significant demographic undergoing DEXA scans at our center. The quantum of data available on males would not have been sufficient to draw a statistically significant conclusion. Therefore, the conclusions and averages drawn herein may not be useful for interpretation when considering male patients. Despite these limitations, the data contained herein can forward the cause of accurate and timely interpretation of bone mineral data to diagnose and treat conditions associated with bone loss in a prompt and effective manner.

CONCLUSION

With the ever-increasing use of BMD scan for a plethora of indications (and the ongoing scenario, where many BMD scans are done at the behest of the patient, to know if they have "adequate bone strength") knowing what is normal is critical to interpretation and implementation of corrective measures. In the Indian scenario, where osteoarthritis is on the rise, the importance of such data cannot be overestimated. Further analyses are required (in the male population, for example) the results of which will help the clinician make meaningful decisions.

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Original Article

Comparative Study of 0.5% Levobupivacaine and 0.5% Levobupivacaine with Fentanyl in Transurethral Resection of Prostate

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Abstract

Background: Subarachnoid block is the most commonly used mode of anesthesia in transurethral resection of prostate. Addition of fentanyl helps in early ambulation and prolonging the duration of analgesia.

Aims and Objectives: To compare the onset and duration of motor and sensory block and duration of analgesia with levobupivacaine alone and in combination with fentanyl.

Materials and Methods: A total of 80 patients between the age group of 50-70 years of ASA Grades II and III were divided into two groups of 40 each. Subarachnoid block in Group A received 0.5% levobupivacaine 2.5 ml (12.5 mg) + 0.9% Nacl 0.5 ml. Subarachnoid block in Group B received 0.5% levobupivacaine 2.5 ml (12.5 mg) + fentanyl 0.5 ml (25 µg). Baseline vitals, onset and duration of motor and sensory block and duration of analgesia were recorded.

Results: The onset and duration of sensory block were prolonged the fentanyl group. Onset of motor block was delayed, however, duration was prolonged in fentanyl group. The duration for first rescue analgesia was prolonged in the fentanyl group.

Conclusion: Addition of fentanyl to levobupivacaine provides faster recovery from motor block and prolongs the duration for analgesic requirement, both of which help in early ambulation.

Key words: Fentanyl, Levobupivacaine, Spinal anesthesia, Transurethral resection of prostate

INTRODUCTION

Spinal and epidural administration of local anesthetics during transurethral resection of prostate (TURP) produce analgesia, anesthesia and motor block, depending on the volume, concentration and doses of drug used. For the local anesthetics selection, it is known that the agent's onset and duration of action, sensory block level to motor block level and cardiac toxicity should be considered. Levobupivacaine ([2S]-1-butyl-N- [2, 6 -dimethylphenyl] piperidine -2 -carboxamide) is an aminoamide local anesthetic which is the pure S(-) enantiomer of racemic bupivacaine has strongly emerged as a safer alternative for regional anesthesia than its racemic sibling, bupivacaine. Levobupivacaine has been found to be equally efficacious as bupivacaine, but with a superior pharmacokinetic profile[1-3] it may be preferred for spinal anesthesia in elderly also.[4,5] Fentanyl is a synthetic opioid, a tertiary amine and a phenylpiperidine derivative which is 50-100 times more potent than morphine. Fentanyl is a highly selective µ receptor agonist, which is mainly responsible for its analgesic properties. Analgesia is produced principally through interaction with µ receptors at supraspinal sites. Fentanyl also binds to K receptors causing spinal analgesia, sedation, and anesthesia.[6]

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Aims and Objectives

To compare the efficacy of levobupivacaine 0.5% and levobupivacaine 0.5% with fentanyl as an adjuvant to study:

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- Onset and duration of sensory block
- Onset and duration of motor block
- Duration of post-operative analgesia.

MATERIALS AND METHODS

After obtaining Institutional ethical clearance and written informed consent from the patients, 80 patients of ASA II and III grade posted for TURP surgery at SRMSIMS, Bhojipura, Bareilly, U.P., were included in the study. A statistician was consulted and method of randomization, adequacy of sample size, and power of test were confirmed. 80 male patients in the age group of 50-70 years undergoing elective TURP surgery of ASA status II and III were selected. Patients were divided into two groups of 40 each. Subarachnoid Block in Group A received 0.5% levobupivacaine 2.5 ml (12.5 mg) + 0.9% Nacl 0.5 ml. Subarachnoid block in Group B received 0.5% levobupivacaine 2.5 ml (12.5 mg) + fentanyl 0.5 ml (25 μg).

Exclusion Criteria

- History of drug hypersensitivity to local anesthetics
- Blood coagulation disorder
- Spinal deformities, raised intracranial tension
- Local sepsis.

A detailed preanesthetic evaluation was carried out for each patient with relevant laboratory and radiological investigations. All patients were visited a day before the surgery and explained in detail the anesthetic procedures and an informed written consent was obtained. All patients were kept nil orally before the day of surgery and received tablet ranitidine 150 mg and tablet alprazolam 0.5 mg both orally as premedication on the night before surgery. On the day of surgery, in the pre-operative preparation room IV line was secured with 18G cannula. Vital parameters such as heart rate, noninvasive arterial blood pressure, SPO2 were monitored. Continuous electrocardiogram (lead II) monitoring was done with the chest leads connected to patients. Baseline readings were recorded. Under aseptic precautions subarachnoid block was given at L3-L4 interspace using 25 G spinal needle in sitting position. The drug was injected into the subarachnoid space according to group assigned after noting the clear free flow of cerebrospinal fluid and given over 10-15 s with the operation table kept flat. Patients were made supine immediately. Oxygen was administered through mask. Vital parameters such as BP, HR, SpO_2, and RR were monitored every 5 min for 45 min. Postoperatively, the time for rescue analgesia was when patient complained of pain at surgical site, which was recorded and treated with suitable analgesics.

Statistics

Data were entered using Microsoft Excel 2010 and statistical analysis was done using IBM SPSS v 20.0.0. Categorical variables were analyzed using proportions and percentages. Continuous variables were summarized by mean and standard deviation. Association between continuous variables was established by parametric tests with 95% confidence intervals where applicable.

RESULTS

The characteristics of the three groups were comparable in terms of age, weight, weight of prostate, and duration of surgery. The onset of sensory block was delayed in Group B (3.15±0.362) as compared to Group A (2.05±0.2207). This was statistically significant. The duration of sensory block was delayed in Group B (361.3±3.22) as compared to Group A (334.1±10.65), which was statistically significant. The onset of motor block was delayed in Group B (4.3±0.464 min) as compared to Group A (3.2±0.4051 min). This was statistically significant but clinically not significant because the difference was of only 66 s, i.e., 1.1 min. The duration of motor block was prolonged in Group A (167.3±3.345) min as compared to Group B (145.2±3.35 min). Analysis was done using "independent *t*-test" which showed a statistically and clinically significant difference between the two groups. *Z*-test of proportion showed that the effective duration of analgesia assessed by duration between the time of establishment of spinal anesthesia to time of first request of rescue analgesia was significantly prolonged in Group B (214.65±8.511) when compared to Group A (121.6±3.82).

Mean age of both groups was compared applying "*Z*-test of proportion" and showed no statistically significant difference (Table 1 and Figure 1).

Mean weight of both groups was compared using "*Z*-test of proportion" and showed no statistically significant difference (Table 2 and Figure 2).

Mean weight of prostate of both groups was compared using "*Z*-test of proportion" and showed no statistically significant difference (Table 3 and Figure 3).

Mean duration of surgery of both groups was compared using "*Z*-test of proportion" and showed no statistically significant difference (Table 4 and Figure 4).

The onset of sensory block was delayed in Group B (3.15±0.362) as compared to Group A (2.05±0.2207). On comparison, using t-test of proportion, a statistically

significant difference was found between the two groups (Table 5 and Figure 5).

The duration of sensory block was delayed in Group B (361.3±3.22) as compared to Group A (334.1±10.65). On comparison, using *t*-test of proportion, a statistically significant difference was found between the two groups (Table 6 and Figure 6).

The onset of motor block was delayed in Group B (4.3±0.464 min) as compared to Group A (3.2±0.4051 min). On comparison, using *t*-test of proportion, a statistically significant difference was found between the two groups. This was clinically not significant because the difference was of only 66 s, i.e., 1.1 min (Table 7 and Figure 7).

Table 1: Comparison of mean age

Parameters	Mean±SD		Z	P
	Group A (*n*=40)	Group B (*n*=40)		
Age (years)	63.23±8.43	63.93±8.24	−0.3756	0.7072

SD: Standard deviation

Table 2: Comparison of mean weight

Parameters	Mean±SD		Z	P
	Group A (*n*=40)	Group B (*n*=40)		
Weight (Kg)	62.84±4.60	63.88±4.48	−1.0244	0.3057

SD: Standard deviation

Table 3: Comparison of mean weight of prostate (g)

Parameters	Mean±SD		Z	P
	Group A (*n*=40)	Group B (*n*=40)		
Weight of prostate (g)	40.28±6.02	39.48±7.15	0.5413	0.5883

SD: Standard deviation

Table 4: Comparison of duration of surgery (min)

Parameters	Mean±SD		Z	P
	Group A (*n*=40)	Group B (*n*=40)		
Duration of surgery (min)	46.82±5.93	46.60±7.32	0.1477	0.8826

SD: Standard deviation

Table 5: Comparison of onset of sensory block (min)

Parameters	Mean±SD		Z	P
	Group A (*n*=40)	Group B (*n*=40)		
Sensory block	3.15±0.362	2.05±0.2207	16.4091	<0.0001(S)

SD: Standard deviation

The duration of motor block was prolonged in Group A (167.3±3.345 min) as compared to Group B (145.2±3.35 min). Analysis was done using "independent *t*-test" which showed a statistically and clinically significant difference between the two groups (Table 8 and Figure 8).

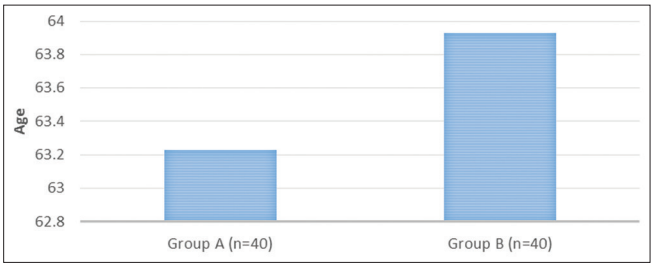

Figure 1: Multiple bar diagrams showing comparison of age in study groups

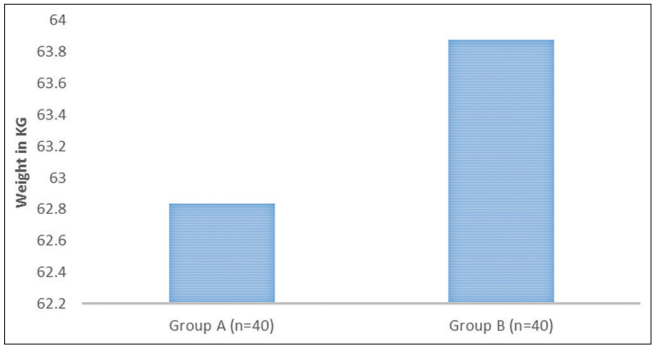

Figure 2: Weight (kg)

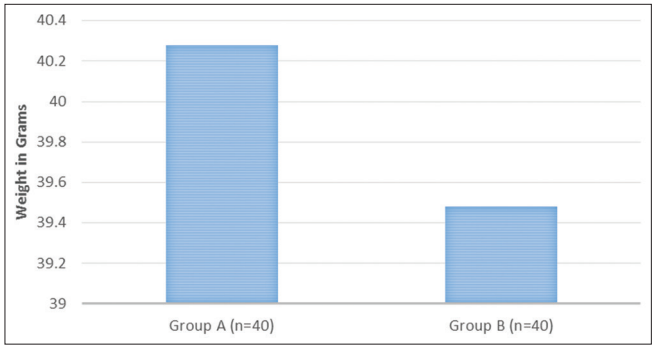

Figure 3: Weight of prostate (g)

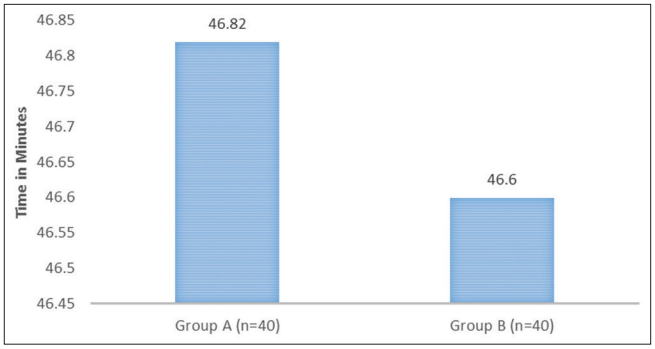

Figure 4: Duration of surgery (min)

Post-operative analgesia was assessed by time for rescue analgesia. *Z*-test of proportion showed that the effective duration of analgesia assessed by duration between the time of establishment of spinal anesthesia to time of first request of rescue analgesia was significantly prolonged in Group B (214.65±8.511) when compared to Group A (121.6±3.82) (Table 9 and Figure 9).

Thus, it is statistically proved that Group B patients had better and long lasting post-operative analgesia than Group A patients.

DISSCUSSION

Adequate anesthesia and good relaxation of the pelvic floor and the perineum, early recognition of signs and symptoms of water intoxication and fluid overload and accidental bladder perforation make subarachnoid block the procedure of choice for TURP surgeries.

The most common serious side effects from spinal anesthesia are hypotension and bradycardia.[7] Hence, if a drug which itself produces intense analgesia without any sympathetic blockade, is available and is added to levobupivacaine, then it will reduce the hemodynamic

Table 6: Comparison of duration of sensory block (min)

Parameters	Mean±SD		*Z*	*P*
	Group A (*n*=40)	Group B (*n*=40)		
Duration of sensory block	334.1±10.65	361.3±3.22	−15.4616	<0.0001

SD: Standard deviation

Table 7: Comparison of onset of motor block (min)

Parameters	Mean±SD		*Z*	*P*
	Group A (*n*=30)	Group B (*n*=28)		
Motor block	3.2±0.4051	4.3±0.464	−11.2947	<0.0001

SD: Standard deviation

Table 8: Comparison of duration of motor block (min)

Parameters	Mean±SD		*Z*	*P*
	Group A (*n*=40)	Group B (*n*=40)		
Duration of motor block	167.3±3.345	145.2±3.35	29.5248	<0.0001

SD: Standard deviation

Table 9: Comparison of time for rescue analgesia (duration of effective analgesia)

Parameters	Mean±SD		*Z*	*P*
	Group A (*n*=40)	Group B (*n*=40)		
Time (h)	121.6±3.82	214.65±8.511	−63.0831	<0.0001

SD: Standard deviation

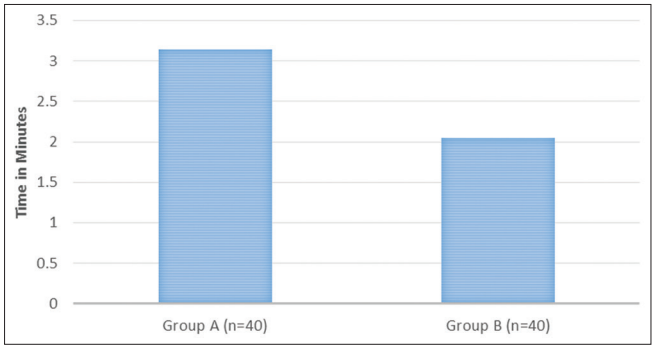

Figure 5: Onset of sensory block

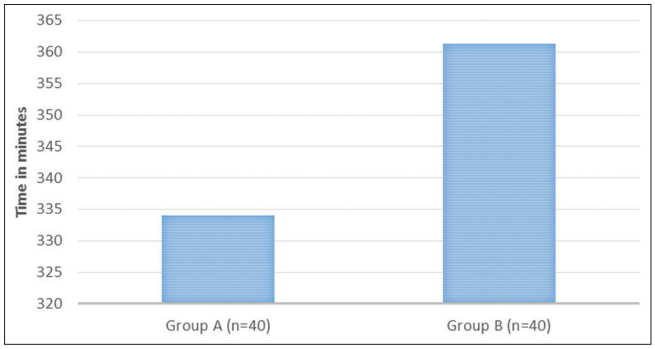

Figure 6: Duration of sensory block

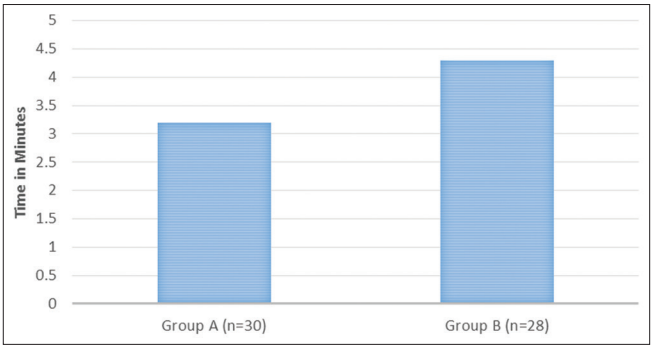

Figure 7: Onset of motor block

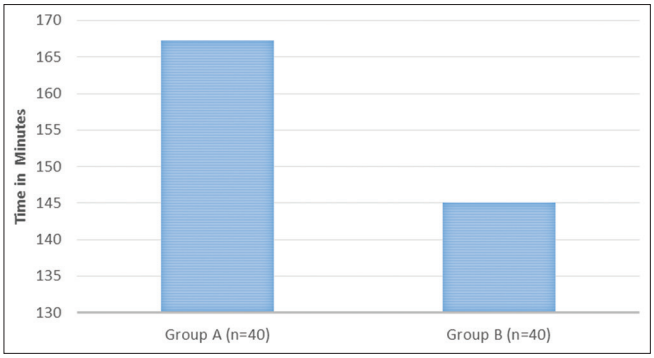

Figure 8: Duration of motor block

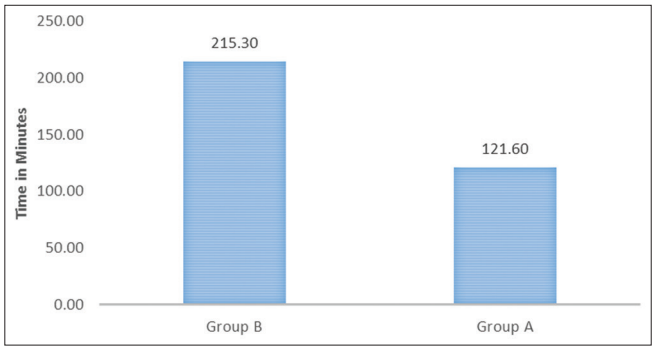

Figure 9: Post-operative analgesia

instability. In this context, spinal opiates have been of much interest in recent times because of their local anesthetic sparing effect. Fentanyl, a synthetic opioid which is 100 times more potent than morphine, having greater lipid solubility, has the quickest onset of action and is, therefore, suitable as an additive to isobaric levobupivacaine when used intrathecally.

Spinal opiates thus administered not only potentiate and reduce the dose local anesthetic agents but also act as post-operative analgesics, because their duration of action is generally longer than that of levobupivacaine.

In our study, the onset of sensory block was delayed in Group B (3.15±0.362) as compared to Group A (2.05±0.2207). The duration of sensory block was delayed in Group B (361.3±3.22) as compared to Group A (334.1±10.65). The onset of motor block was delayed in Group B (4.3±0.464 min) as compared to Group A (3.2±.4051 min). The duration of motor block was prolonged in Group A (167.3±3.345 min) as compared to Group B (145.2±3.35 min).

This shows that addition of fentanyl to levobupivacaine delays onset of sensory and motor block which is clinically insignificant and practically acceptable.

It prolongs the duration of sensory block but reduces the duration of motor block which is favorable for TURP surgeries as it helps in early mobilization.

Cuvas *et al.*[5] conducted a study on spinal anesthesia for transurethral resection operations: Levobupivacaine with or without fentanyl in 2010. It concluded that both regimes were effective and the addition of fentanyl to levobupivacaine offers the advantage of shorter duration of motor block and maybe used as an alternative to pure levobupivacaine for TURP.

Akan *et al.*[8] conducted a study on comparison of levobupivacaine alone and in combination with fentanyl and sufentanil in patients undergoing transurethral resection of the prostate in 2013. It concluded that combining lower dose levobupivacaine with fentanyl and sufentanil provided faster onset of sensorial block, lower frequency and shorter duration of motor block, and longer analgesia time in TURP under spinal anesthesia.

Brahmbhatt *et al.*[9] conducted a study on combination of low dose isobaric levobupivacaine 0.5% and fentanyl compared with isobaric levobupivacaine 0.5% in spinal anesthesia for lower abdominal and perineal surgeries in 2015. It concluded that combination of intrathecal fentanyl with low dose levobupivacaine provides good surgical anesthesia but early motor recovery which is well suited for outpatient anesthesia.

In this study, the mean duration of analgesia in fentanyl group was 214 min which was significantly prolonged compared to levobupivacaine group where patients had effective analgesia only up to about 121 min.

These findings are very well complimented by following previous studies.

Akan *et al.*[8] conducted a study on comparison of levobupivacaine alone and in combination with fentanyl and sufentanil in patients undergoing transurethral resection of the prostate in 2013. It concluded that addition of fentanyl to levobupivacaine in spinal anesthesia prolonged the duration of analgesia in TURP surgeries.

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CONCLUSION

We have concluded that it is safe to use levobupivacaine alone or with fentanyl as an adjuvant in ASA III patients. The addition of 25 mcg of fentanyl to levobupivacaine 15 mg in contrast to levobupivacaine 15 mg does not clinically significantly compromise with onset of sensory and motor block. It delays the onset and prolongs the duration of sensory block and shortens the duration of motor block. This is beneficial for early ambulation of patients. Duration of post-operative analgesic requirement was better in the levobupivacaine with fentanyl group as compared to levobupivacaine which was also statistically significant.

Hence, fentanyl added to levobupivacaine provides good prolonged post-operative analgesia and provides early ambulation in TURP surgeries.

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Original Article

Ventilator Associated Pneumonia-Incidence and Outcome in Adults in Medical Intensive Care Unit of a Tertiary Care Hospital of North India

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Abstract

Background: Various studies reveal that pneumonia complicates a majority of patients in intensive care units (ICUs) who are on invasive mechanical ventilation (MV). Up to 50% of such patients die of this disease, however, the mortality varies in different population groups, different underlying indicator diseases and also among different ICUs. This study was carried out to observe the profile of ventilator associated pneumonia (VAP) and its mortality among our patients, as per age and sex, admitted in the ICU of a tertiary care hospital.

Methods: A 14 months study of admitted patients was conducted in our ICU to see the pattern of pneumonia among ventilated patients. VAP was diagnosed according to clinical pulmonary infection score (CPIS) scoring system where a score > or =6 was taken as significant.

Results: The study showed that among a total of 178 patients admitted in the ICU, 92 (51.68%) were managed with invasive MV. Out of these 92 patients, 12 (13.04%) developed VAP as per CPIS scoring system. Out of 12 patients, 6 died, revealing 50% mortality among VAP patients.

Conclusion: VAP occurred in our ICU setup in 13.04% patients on MV over a period of 13-month with a VAP rate of 17.09/1000 days on MV. The mortality among VAP patients in our ICU was 50% in comparison to overall mortality of 48.91% in all mechanically ventilated patients.

Key words: Incidence, Intensive care unit, Mechanical ventilation, Mortality, Ventilator associated pneumonia

INTRODUCTION

Ventilator-associated pneumonia (VAP) is defined as pneumonia occurring more than 48 h after patients have been intubated and received mechanical ventilation (MV). However, the appropriate definition of VAP is subjective as significant variability among observers is noted.[1,2] VAP is classified as early- and late-onset disease occurring during the first 4 days or beyond 4 days of patient admission. Pneumonia is the second most common nosocomial infection in critically ill patients, affecting 27% of all critically ill patients.[3] 86% of nosocomial pneumonia are associated with MV and are termed VAP. VAP typically affects critically ill persons that are in an intensive care unit (ICU).[4] Persons with VAP have increased lengths of ICU hospitalization and have up to a 20-30% death rate.[5] The mortality attributable to VAP has been reported to range between 0% and 50% in various studies.[6-10] As shown by Hunter, VAP occurs in 9-27% of mechanically ventilated patients, with about five cases per 1000 ventilator days.[11] The condition is associated with increased ICU and hospital stay and has an estimated attributable mortality of 9%.[11] According to Chastre and Fagon, despite major advances in techniques for the management of ventilator-dependent patients and the routine use of effective procedures to disinfect respiratory equipment, VAP continues to

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complicate the course of 8-28% of the patients receiving MV.[12] Rates of pneumonia are considerably higher among patients hospitalized in ICUs compared with those in hospital wards, and the risk of pneumonia is increased 3- to 10-fold for the intubated patient receiving MV.[12] The chance of getting VAP has been described as 3% per day during the first week of MV, 2% per day during the second week and 1% per day in the ensuing weeks.[13] VAP occurrence is also increased with prolonged length of ICU stay.[14,15] A method to reduce the risk of VAP is to extubate patients as soon as possible as various randomized, and observational studies have shown that the risk of developing VAP increases with the duration of an endotracheal tube remaining in place.[16] The use of appropriate weaning protocols and the regular assessment of sedation requirements are effective in reducing the duration of MV and hence the incidence of VAP.[17-20] VAP must be suspected clinically in an ICU setting, and quick assessment must be done for its diagnosis as the delay can increase both morbidity and mortality among such patients. Delays in the administration of appropriate antibiotic therapy for VAP have been associated with excess mortality.[21-23] In one study, a delay in appropriate therapy for 24 h or more was associated with a 69.7% mortality, compared to 28.4% in patients treated without the delay ($P < 0.001$).[22] Hence, a prompt decision needs to be taken, and antibiotics must be started empirically, which can later be changed as directed by the culture and sensitivity reports. According to Luna *et al*., mortality rates vary with patient population and infecting organism, mortality increasing when the infecting organism is multidrug resistant.[24] The probability for multi-drug resistant pathogens is higher in the subset of patients including those recently hospitalized in acute care facility (<90 days), residents in a nursing home or long-term care facility; recipients of recent intravenous antibiotic therapy, chemotherapy, or wound care within the last 30 days of the current infection; or who have attended a hospital or hemodialysis clinic.[25] Starting appropriate antibiotics is a simple and effective way to improve clinical outcomes while minimizing side effects and maintaining quality of care.[26,27] Above all, education of health-care personnel is important and is widely viewed as a fundamental step in reducing the occurrence of VAP.[25,28]

METHODS

A prospective observational study of admitted patients was conducted in our medical ICU over a period of 14-month from October 2014 to December 2015 to see the pattern of pneumonia among ventilated patients. Besides routine investigations, we did the tracheal aspirate cultures with sensitivity in these patients. The progressive monitoring of chest radiographs was also performed. VAP was diagnosed according to clinical pulmonary infection score (CPIS) scoring system where a score > or = 6 was taken as significant. The calculation of CPIS is shown in Table 1.

Statistical Analysis

Data were analyzed using EpiInfo 7.0. Relationship between two categorical variables was analyzed using Chi-square test. Two-sided *P*-values were reported and a $P < 0.05$ was considered statistically significant.

RESULTS

The study showed that among a total of 178 patients admitted in the ICU, 92 (51.68%) were managed with invasive MV. Out of these 92 patients, 12 (13.04%) developed VAP as per CPIS scoring system with a VAP rate of 17.09/1000 days on MV. Out of 12 patients, 6 died, revealing 50% mortality among VAP patients. The results obtained are tabulated in Table 2.

A total number of patients admitted to the ICU were 178 out of whom 92 (51.68%) were put on invasive MV. Out of the admitted patients, 100 were males and 78 were females. 44 male patients and 48 females were put on MV. VAP

Table 1: CPIS calculation

Parameters	Points
Temperature, °C	
≥36.1 and ≤38.4	0
≥38.5 and ≤38.9	1
≥39.0 and ≤36.0	2
Blood leukocytes, mm^3	
≥4,000 and ≤11,000	0
<4,000 or >11,000	1
+Band forms ≥50%	Add 1
Tracheal secretions	
Absence of tracheal secretions	0
Presence of non-purulent tracheal secretions	1
Presence of purulent tracheal secretions	2
Oxygenation: PaO_2/FiO_2, mmHg	
>240 or ARDS (defined as PaO_2/FiO_2≤200, PCWP ≤18, and acute bilateral infiltrates)	0
≤240 and no ARDS	2
Pulmonary radiography	
No infiltrate	0
Diffuse (or patchy) infiltrate	1
Localized infiltrate	2
Progression of pulmonary infiltrate	
No radiographic progression	0
Radiographic progression (after CHF and ARDS excluded)	2
Culture of tracheal aspirate	
Pathogenic bacteria cultured in rare or light quantity or no growth	0
Pathogenic bacteria cultured in moderate or heavy quantity	1
+Same bacteria seen on Gram-stain	Add 1
Total score	

Reference: Am J Respir Crit Care Med 2000;162:505-11. ARDS: Acute respiratory distress syndrome, CHF: Congestive heart failure, PaO_2/FiO_2: Ratio of arterial oxygen pressure to fraction of inspired oxygen, PCWP: Pulmonary capillary wedge pressure

developed in 6 out of 44 males and in 6 out of 48 females. Tracheal aspirates were taken in the 12 patients who developed VAP. Out of these 12, 7 aspirates were positive, of which 5 grew *Acinetobacter* species, 1 was positive for *Pseudomonas aeruginosa* and other for *Klebsiella*. The sensitivity patterns showed maximum sensitivity for colistin and amikacin. 4 males and 2 females with VAP died. Thus, a total of 12 out of 92 ventilated patients developed VAP and 6 died. VAP was seen in patients who were on MV for at least 1 week.

DISCUSSION

This study showed that among patients admitted in the ICU, 51.68% were managed with invasive MV. Out of these, 13.04% developed VAP with a VAP rate of 17.09/1000 MV days, and 50% was the mortality among VAP patients.

The duration of MV affects the occurrence of VAP. As per the study by Cook in 2000, VAP occurs most often in the first week of MV.[5] Fagon *et al*. suggested that the incidence of VAP increases by 1% per day of IMV.[29] However, Cook *et al*., in 1998, found that the incidence per day varies over time, with 3% per day during first 5 days of IMV, 2% for the second 5 days, and 1% for the subsequent 5-day period.[30] This observation is supported by Ibrahim *et al*., who identified an incidence rate of VAP of 11.5%, 56% of which were early onset (≤5 day).[31] Hence, the greatest attack rates appear to be during the initial days of MV. In addition, significant risk factors for early-onset VAP include cardiopulmonary resuscitation and continuous sedation.[32] In our study, VAP was seen in patients who were on MV for at least 1 week, and VAP occurrence showed an increasing trend with the increase in duration of ventilation (Table 3). There is some evidence for gender differences in the course of VAP: Men have been found to get VAP more often, but women are more likely to die after contracting VAP.[33] In our study, 44 male patients (out of 100) and 48 females (out of 78) were put on MV. VAP developed in 6 out of 44 males and in 6 out of 48 females. 4 males and 2 females with VAP died (Table 4).

In summary, all possible steps should be taken to decrease the incidence of VAP in ICUs. Clinicians must focus on eliminating or minimizing the incidence of VAP through preventive techniques. The focus should be addressing modifiable risk factors.[34-39] Zack *et al*. have demonstrated that a multifaceted and multidisciplinary approach to VAP prevention can indeed reduce the incidence.[40]

CONCLUSION

In our ICU setup, VAP occurred in 13.04% of mechanically ventilated patients admitted over a period of 14-month with a VAP rate of 17.09/1000 days on MV. The mortality among VAP patients in our ICU was 50%. VAP was seen in patients who were on MV for at least 1 week and VAP occurrence showed an increasing trend with the increase in duration of ventilation. More males developed and died from VAP as compared to females. Keeping into consideration the burden of increased morbidity, lengthening of ICU stay and increased mortality due to VAP, We recommend that appropriate measures ensuring application of VAP bundle, hand hygiene, and proper suctioning methods be employed to reduce the prevalence of VAP in ICU.

Table 2: Gender distribution of VAP among admitted ICU patients

Gender	Number of cases	VAP	Percentage of VAP	*P*-value
Male	100	6	6.00	0.655
Female	78	6	7.69	
Total	178	12	6.74	

VAP: Ventilator-associated pneumonia, ICU: Intensive care units

Table 3: Distribution of VAP cases as per the duration of ventilation

Days on ventilator	Number of cases	VAP	Percentage	*P*-value
<15	83	7	8.43	<0.001
>15	9	5	55.55	
Total	92	12		

VAP: Ventilator-associated pneumonia

Table 4: Outcome of VAP versus non-VAP among ventilated patients

Outcome	Total VAP	Non-VAP	*P*-value
Expired	6	38	0.872
Survived	6	42	
Total	12	80	

VAP: Ventilator-associated pneumonia

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Original Article

Master Health Check-up Attendees in High Risk Group for Sexually Transmitted Infections over a Period of 15-Month in a Tertiary Care Hospital: A Retrospective Study

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Abstract

Introduction: High risk group (HRG) for sexually transmitted infections (STI) includes female sex workers (FSW), transgender (TG) with high risk behavior, and homosexual's men having sex with men (MSM). They have high risk of being infected with STI and HIV.

Aims: To estimate the prevalence of high risk individuals in Tirunelveli, to compare the number of high risk individuals turning up to STD OPD during master health check-up period and previous years, to assess the type of STI in each HRG, and to estimate venereal disease research laboratory (VDRL), HIV and VIA-VILI positivity among master health check-up attendees.

Methods: Master health check-up was conducted at STD OPD, Tirunelveli Medical College Hospital, Tirunelveli. With the help of non-governmental agencies, all the people with high risk behavior were recruited for master health check-up during the stipulated time of 15 months and detailed history was taken, physical and genital examination was done. Investigation for HIV, syphilis, and other sexually transmitted diseases were also done.

Results: A total of 474 HRG turned up, among them, 384 were male, 86 were FSW, and 4 were TG. About 14 cases among HRG were VDRL positive and 9 were positive for HIV (all of them were MSM) and 1 case (of FSW) was positive for VIA-VILI. The most common STI symptom found in these MSM was burning micturition followed by itching over the genitals. Trichomoniasis is the common sexually transmitted disease affecting the FSW and it is present in about 5 cases. The next common infection present in them was bacterial vaginosis, which was found in 3 cases. All the 4 TG were asymptomatic and non-reactive for ICTC and VDRL.

Conclusion: Among all the HRGs, the STI burden was high in the male having sex with males. Syphilis is the most common infection affecting male homosexuals. Trichomoniasis is the common cervico-vaginal discharge syndrome affecting the FSW. TG, in this study, was asymptomatic and seronegative.

Keywords: Bacterial vaginosis, Female sex workers, HIV, Male having sex with males, Master health check-up, Syphilis, Transgender, Trichomoniasis

INTRODUCTION

High risk group (HRG) is a group of people in the community with a higher than expected risk for developing a particular disease. HRG for sexually transmitted infections (STI) includes men having sex with men (MSM),[1] female sex workers (FSW), and transgender (TG).

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Male Having Sex with Male

Also called as homosexuals, i.e., a person who predominately or exclusively has sex with a person or persons of same sex.[2] These MSM have a higher prevalence of STI due to the following reasons:[3]

a. Male possess penis, which is a penetrative organ. Penis is designed to transmit semen along with infectious organisms if present in the seminal fluid.
b. The highly receptive columnar epithelial surface is involved in male to male sex, which includes

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rectal mucosa, anorectal squamocolumnar junction, oropharyngeal and tonsillar mucosa, inner surface of prepuce.

Any breach in these surfaces favors transmission of infection from one person to another.[4]

FSW

A sex worker is a person who is employed to provide direct sexual services for the purpose of money or goods. In the case of FSW, the clients are always male. The unequal power differences between the sexes prevent them from effectively negotiating condom use and safe sex, thereby increasing the risk of transmission of STI. Sex trade is regulated by law which is often biased against women thereby pushing sex workers to live at the margins of the society. This unequal gender and social status affects their self-esteem and confidence to access and utilize relevant STI-related services including social entitlements.

TG

A TG is a person, who dresses as, desires to be, has undergone a surgery to become or identifies as a person of opposite sex. A disproportionate number of TG finds employment in the sex industry because of discrimination and subsequent financial hardship. In some countries, it is the only way for the TGs to earn money and to afford hormonal and surgical treatments. Also because of the stigmatization in the sex industry, they are more likely to engage in unprotected intercourse.[5]

STI as cofactor and frequent unprotected sex puts these HRG at increased risk of acquiring and transmitting STIs and HIV to clients and other partners.[6] Although they are one of the groups most affected by STD and most likely to respond well to STI prevention programs, they are also the people who do not seek medical services. Hence, preventive programs should target this HRG for effective reduction in STI. This needs identification and knowing the true prevalence of HRG in the community, so regular screening and testing can be done and treatment of concurrent STI can be ensured, thus decreasing the transmission which is essential in implementing any sexual health-care program.

MATERIALS AND METHODS

Master health check-up was conducted in STD outpatients department at Tirunelveli Medical College Hospital, Tirunelveli. With the help of non-governmental agencies (NGO), all the people with high risk behavior were recruited for master health check-up during the stipulated time of 15 months and detailed history taking including history of burning micturition and urethral discharge, genital ulcer or vesicle or painful genital lesion or swelling in the genitalia were enquired of, in either genders, and h/o abnormal vaginal discharge and lower abdominal pain (LAP) was asked in females. H/o oral and perianal lesions were enquired.

Exposure history including marital, premarital, and extramarital contact were asked. Types of exposure-active/passive, insertive/receptive, urogenital, and anogenital were also enquired. The patients were ensured about the confidentiality of the clinical data. After obtaining consent from the patient, thorough physical examination including examination of genitals, perianal region, oral mucosa, palms and soles, bones and joints, and skin examination were also performed.

Speculum examination is done for visualization of vagina and cervix in female, swabs taken from vagina and cervix for saline mount, grams stain, KOH mount, and examined under microscope and whiff test was done. For males proctoscopy was done to visualize anal canal and patulous anus if present was noted. Moreover, swab for gram stain was taken in cases with urethral discharge and anorectal discharge. Blood Investigation for HIV, syphilis, and other sexually transmitted diseases were also done with the consent of the patient.

RESULTS

Patients screened during the study are 474, of which 384 were male homosexuals, 86 were FSW, 4 were TG. 21% of the OPD were HRG during the MHC period. Among these HRG, 14 were found to be RPR positive and they were all MSM and 9 cases were positive for HIV, and they were also only MSM 1 case of CSW was positive for VIA-VILI (Table 1).

The total number of cases who attended the OPD during the study period was 2310 of which 78 cases were HRG. Among them 48 were male homosexuals, 29 were FSW, 1 was TG. 3.3% of the OPD patients were HRG.

During the MHC period, a total of 474 cases of HRG were recruited with the help of TI-NGOs, whereas in the same period during the previous year, only 78 HRG had turned up to STI OPD. This shows that MHC has increased the

Table 1: VDRL, HIV, VIA-VILI positivity in HRG

Total number of cases	Male homosexuals	Female sex workers	Transgender	Total
	384	86	4	474
Total VDRL positive	14	-	-	14
Total HIV positive	9	-	-	9
VIA-VILI positive	-	1	-	1

VDRL: Venereal disease research laboratory, HRG: High risk group

recruitment of HRG about seven times than that during normal OPD. The occurrence of syphilis and HIV in HRG is 2.9% and 1.8%, respectively, whereas in the normal OPD, it is only 0.17% and 0.13%, which is more than 10 times higher occurrence than the normal population. This indicates that syphilis and HIV were found higher in the HRG. Among 86 FSWs, 10 cases were symptomatic with complaints of cervico-vaginal discharge (CVD) and LAP. Of them, 8 cases presented with both CVD and LAP and 7 had severe itching of genitals. Total number of symptomatic cases in FSW = 10 (Table 2).

On speculum examination of 5 cases had CVD, LAP and severe itch, a profuse frothy, yellowish green discharge was seen in the vagina. Microscopic examination of saline mount showed jerky motile organisms, and they were diagnosed to have trichomoniasis. 3 cases had bacterial vaginosis, which was confirmed by whiff test and gram staining, which showed the presence of more than 20% of vaginal epithelial cells as clue cells in cytology. Clue cells are vaginal epithelial cells, studded with numerous bacteria, both gram positive and negative both aerobic and anaerobic, obscuring the margin of epithelial cells. 2 cases with only CVD were diagnosed to have vulvovaginal candidiasis by saline mount and KOH preparation. Among 384 male homosexuals, 9 were symptomatic. The most common STI symptom found in MSM were burning micturition (5 cases), followed by itching over the genitals (2 cases) (Table 3).

Also on physical examination, smegma (due to poor genital hygiene) was seen in 3 cases, phimosis was present in 3 cases due to balanoposthitis, and patulous anus was found in 2 cases who were engaged in receptive anal intercourse. All the 4 cases of TG were asymptomatic and were ICTC and venereal disease research laboratory negative.

Table 2: Symptoms seen in FSWS

Symptoms	Number of cases
LAP+CVD	8
CVD only	2
LAP+CVD+severe ITCH	5

LAP: Lower abdominal pain, CVD: Cervico-vaginal discharge

Table 3: Symptoms present in MSMS

Symptoms	Number of cases
Venereal symptoms	
Burning micturition	5
Itching over the genitals	2
Premature ejaculation	1
Nocturnal emission	1
Non-venereal dermatosis	
Intertrigo	5
Scabies	2
Scrotal eczema	1
Vitiligo on prepuce	1
Non-venereal surgical conditions	
Inguinal hernia	1
Hydrocele	1
Others	
Smegman	3
Phimosis	3
Patulous anus	1

MSM: Men having sex with men

DISCUSSION

HRG formed 21% of STD OP population during the master health check-up period, whereas during the same period in the previous year, they contributed only to 3.3% of the OPD. There was seven-fold increase in population of HRG group attending STD clinic for master health check-up. The occurrence of syphilis and HIV in HRG is 2.9% and 1.8%, respectively, whereas in the normal OPD, it is only 0.17% and 0.13%, which is more than 10 times higher occurrence than the normal population. This indicates that syphilis and HIV were found higher in the HRG. This is similar to the study conducted by Malta *et al.* in Brazil.[7] In this study, about 2.9% of HRG were found to have affected by syphilis. In a similar study conducted at Nanjing in China, syphilis is the most common infection among the HRG (10.3%). Both studies conclude that syphilis was found in a greater percentage in high risk population.[8] And about 1.8% of HRGs were affected by HIV, which is more than 10 times higher occurrence than the normal population. Only 0.2% of them were positive for VIA-VILI. All the cases of HRG who were positive for HIV and syphilis in my study belonged to male having sex with males, and all the FSW and TG were non-reactive for both HIV and syphilis. This is similar to the study done by Hawkes *et al.* in Pakistan, where no FSW had HIV prevalent in them.[9] The most common cervico-vaginal discharge syndrome among the CSW in this study was trichomoniasis which is 0.5%, followed by bacterial vaginosis (0.3%) and candidiasis (0.2%). This is in contrast to the study by Alvis *et al.*, where bacterial vaginosis was the common followed by *Chlamydia trachomatis*, *Neisseria gonorrhoeae*, *Trichomonas vaginalis,* and *Candida albicans* in that order.[10] In MSM, the most common STI symptom was burning micturition, which is present in about 1.3% of the cases. The second common symptom is itching over the genitals, present in about 0.5% of cases and premature ejaculation and nocturnal emission were present in about 0.2% of the cases. Intertrigo is the most common non-venereal dermatosis found in about 1.3% of the MSM. Other non-venereal dermatosis found in MSM was scabies (0.5%), vitiligo on prepuce (0.5%), and scrotal eczema (0.2%). On physical examination, smegma and phimosis is present in about 0.7% and patulous anus in about 0.5%

of them. Other non-venereal surgical conditions present in MSM include inguinal hernia (0.2%) and hydrocele (0.2%). All the syphilis cases in this study were MSMs. 3.64% of MSMs were positive for syphilis. This is in contrast to the study by Bleeker *et al.*, where 36% of the MSMs were positive for syphilis. The difference may be due the period of the study which was in early 1980s.[11] All the TG were asymptomatic and seronegative for both HIV and syphilis. Master health check-up has caused a sevenfold increase in number of HRG attending STD OPD which is very significant. HIV and syphilis seroreactivity was seen the highest in male having sex with males.[12]

CONCLUSION

This study had concluded that master health check-up had resulted in significant increase in the number of high risk individuals turning up to STD OPD. Thus, periodic master health check-up should be conducted to identify HRG and to diagnose them to prevent the STI outbreak in the community.

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Original Article

Effect of Maternal Body Mass Index on Pregnancy Outcome

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Abstract

Introduction: Maternal body mass index (BMI) is one of the most important predictor of nutritional status of pregnant lady. Both nutritional intake and maternal weight are modifiable factors which can influence pregnancy outcome. Either underweight or overweight, both can have significant impact on outcome of pregnancy. Most of the developing countries including India are now facing double burden because of extreme socioeconomic distribution. Obese women are more prone for developing gestational hypertension, preeclampsia, gestational diabetes mellitus, macrosomia, postpartum hemorrhage, and increased incidence of operative deliveries.

Aims and Objectives: To determine the maternal risk in terms of antepartum, intrapartum, postpartum complications and perinatal outcome in relation to extremes of maternal BMI.

Materials and Methods: This was a prospective study conducted for a period of 1 year. Total 150 patients were taken for study after satisfying all inclusion and exclusion criteria. However, 40 patients were excluded from study due to loss of follow-up. All patients were followed up till delivery and various outcomes were studied and analyzed.

Results: A total of 72 (65.45%) patients were in the age group of 21-30 years. Our study has shown that both underweight and overweight women had adverse maternal and perinatal outcome. In underweight group, there was high incidence of anemia which has affected 35% of patients. Low APGAR score and neonatal intensive care unit admissions were more frequent in BMI Group 3, 4, and 5 patients.

Conclusion: It can be concluded from our study that extremes of maternal BMI is associated with adverse maternal and perinatal outcome. Adequate preconceptional counseling should be given to all women in reproductive age group so that they can attain normal BMI before conception.

Key words: Body mass index, Gestational diabetes mellitus, Gestational hypertension, Macrosomia, Obesity, Pregnancy outcome

INTRODUCTION

Maternal body mass index (BMI) is one of the most important predictor of nutritional status of pregnant lady. Both nutritional intake and maternal weight are modifiable factors which can influence pregnancy outcome.[1] Either underweight or overweight both can have a significant impact on outcome of pregnancy.

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Worldwide there has been alarming increase in the incidence of obesity and overweight, particularly in the past two to three decades. In the latest report, the WHO has indicated that approximately 1.6 billion adults are overweight and around 400 million are obese. Obesity as thus becomes a major contributor for global burden of chronic diseases and disabilities.[2]

Most of the developing countries including India are now facing double burden because of extreme socioeconomic distribution. On one side, there is overweight and obesity which has reached epidemic proportions and on the other side there is underweight and undernourishment. In India, 26% of pregnant women are overweight and 8% are obese.[3]

Pregnancy complications secondary to overweight and obesity have been studied from as early as 1945, and it has

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been well established that these women are more prone for developing gestational hypertension, preeclampsia (PE), gestational diabetes mellitus (GDM), macrosomia, postpartum hemorrhage, and increased incidence of operative deliveries.[4,5] Furthermore, it has been showed that low APGAR score and perinatal deaths are more common in neonates of obese women.[6,7] However, effect of underweight remains bit unclear. There are some studies which have reported increased incidence of anemia, intrauterine growth retardation, low birth weight (LBW) babies, and preterm labor. While some studies have reported a protective effect on some pregnancy complications such as GDM and PE.[8] Hence, this study is to determine the effect of maternal BMI on pregnancy outcome.

Aims and Objectives

1. To determine the maternal risk in terms of antepartum, intrapartum, and postpartum complications in relation to extremes of maternal BMI
2. To determine the perinatal outcome in relation to extremes of maternal BMI.

MATERIALS AND METHODS

This was a prospective study conducted at the Department of OBG, Institute of Maternal and Child Health attached to Government Medical College, Kozhikode, for 1 year from March 2012 to February 2013.

Inclusion Criteria

1. Primigravida with singleton pregnancy
2. Booked cases with their first visit before 12 weeks of gestation
3. No history of any medical disorders.

Exclusion Criteria

1. Multipara
2. Multiple pregnancy
3. Presence or history of any medical disorders.

A total of 150 patients were taken for study after satisfying all inclusion and exclusion criteria. However, 40 patients were excluded from study due to loss of follow-up. Hence, sample size of this study was 110. The measurements of height and weight were taken by means of standard methodology described by Lohman *et al.*[9] BMI of patients was calculated using formula:

BMI = (weight in kilograms/height in meters^2).

Based on BMI, patients were divided into five groups (according to the WHO and NIH guidelines).

A complete history regarding present and past illness was noted. Detailed general physical and systemic examination was performed. Baseline routine investigations were performed. All findings were noted down in a predesigned pro forma and records were maintained till delivery. All patients under study were counseled to have follow-up visits as per standard protocol till delivery. Decision regarding mode of delivery was taken depending on the particular case. All the babies were examined by a pediatrician. APGAR scores of the babies were assessed and neonatal intensive care unit (NICU) admissions were recorded.

The obstetrical outcomes studied

- Miscarriage
- Impaired glucose tolerance (IGT), GDM
- Gestational hypertension
- PE, eclampsia
- Anemia
- Preterm delivery
- Mode of delivery
- Postpartum complications.

The neonatal outcomes studied:

- Birth weight
- Maturity
- NICU admission
- Perinatal death.

RESULTS

In our study total 110 patients were studied. In all BMI groups maximum numbers of patients were in the age group of 21 to 30 years (Tables 1-3).

Table 1: Category and group of patients based on BMI

Group	Category	BMI
1	Underweight	≤19.9 kg/m^2
2	Normal	20-24.9 kg/m^2
3	Overweight	25-29.9 kg/m^2
4	Obese	30-34.9 kg/m^2
5	Morbidly obese	≥35 kg/m^2

BMI: Body mass index

Table 2: Number of cases in each group

Group	Category	Number of cases (%)
1	Underweight	32 (29.09)
2	Normal	37 (33.063)
3	Overweight	27 (24.54)
4	Obese	10 (9.09)
5	Morbidly obese	4 (3.63)

Table 3: Age-wise distribution

Group	Age in years		
	≤20	21-30	31-35
1	8	20	4
2	4	28	5
3	3	16	8
4	2	5	3
5	0	3	1
Total (%)	17 (15.45)	72 (65.45)	21 (19.09)

Complications like Gestational hypertension was more common in Group 3,4 and 5. Anaemia was more common in Group 1 (Table 4).

Table 4: Complications during antepartum period

Complications	BMI group (total number of cases) (%)				
	1 (32)	2 (37)	3 (27)	4 (10)	5 (4)
Miscarriage	3 (9.37)	1 (2.7)	2 (7.4)	1 (10)	0
Impaired glucose tolerance	0	5 (13.51)	1 (3.7)	0	0
GDM	0	2 (5.4)	2 (7.4)	0	0
GHT	3 (9.37)	2 (5.4)	4 (14.8)	2 (20)	1 (25)
Preeclampsia	0	1 (2.7)	1 (3.7)	2 (20)	1 (25)
Eclampsia	0	0	0	0	1 (25)
Anemia	10 (31.25)	7 (18.91)	3 (11.1)	1 (10)	1 (25)
Antepartum hemorrhage	0	0	0	1 (10)	0

BMI: Body mass index

Compared to women with normal BMI(Group 2), LSCS rate was more common in Group 2,3,4 & 5. LSCS rate in Group 2,3,4 & 5 was 19.5%, 32%, 44.5% and 25% respectively (Table 5).

Table 5: Mode of delivery

BMI group	1	2	3	4	5	Total
Number of cases (excluding miscarriages)	29	36	25	9	4	103
Normal delivery (%)	25 (86.20)	29 (80.5)	17 (68)	5 (55.5)	3 (75)	79 (76.7)
LSCS (%)	4 (13.8)	7 (19.5)	8 (32)	4 (44.5)	1 (25)	24 (23.3)

BMI: Body mass index, LSCS: Lower segment Cesarean section

Table 6: Postpartum complications

BMI group	1	2	3	4	5
Number of cases (excluding miscarriages)	29	36	25	9	4
Nil complications (%)	22 (75.86)	25 (69.4)	14 (56)	5 (55.5)	2 (50)
Perineal laceration	0	2	3	1	1
Postpartum Hemorrhage	1	0	1	0	0
Urinary tract infection	2	3	4	1	0
Respiratory tract infection	1	2	1	0	0
Wound infection	3	3	3	2	1

BMI: Body mass index

Postpartum complications increased with increase in BMI (Table 6). Macrosomia was more common in Group 5 with mean Birth weight of babies being 3.36 kg (Table 7). Rate of NICU admission was more common in Group 4 and 5 patients(Table 8).

Table 7: Maternal BMI and birth weight of babies

BMI group	1	2	3	4	5
≤2.5 kg	18	3	2	1	1
2.6-3.5 kg	11	19	7	2	0
3.6-3.9 kg	0	14	13	4	2
≥4 kg	0	0	3	2	1
Mean birth weight	2.32	2.94	3.2	3.28	3.36

BMI: Body mass index

Table 8: Maternal BMI, APGAR score, and NICU admission

BMI group	1	2	3	4	5	Total (%)
APGAR score						
1'9	25	31	21	7	3	87 (84.46)
1'<9	4	5	4	2	1	16 (15.53)
NICU admission (%)	6 (20.67)	10 (27.7)	9 (36)	3 (33.3)	2 (50)	

BMI: Body mass index, NICU: Neonatal Intensive Care Unit

Table 9: Neonatal deaths in different groups

BMI group	Number of neonatal deaths	Causes
1	2	Low birth weight, Perinatal asphyxia
2	0	
3	1	Low birth weight, RDS
4	1	MAS, sepsis
5	0	

BMI: Body mass index, RDS: Respiratory distress syndrome, MAS: Meconium Aspiration Syndrome.

DISCUSSION

In our study, 72 (65.45%) patients were in the age group of 21-30 years, which reflects the normal child bearing age group of women.

Our study has shown that both underweight and overweight women had adverse maternal and perinatal outcome. The women who were overweight/obese/morbidly obese had significantly higher risk of gestational hypertension, PE and IGT. Rate of lower segment cesarean section (LSCS) was also higher in these groups. This is in line with other studies like Bhattacharya *et al.*[10]

In underweight group, there was high incidence of anemia which has affected 35% of patients. This is due to lower socioeconomic status and nutritional deficiencies. This

correlates with other studies like Jain *et al.*[11] In our study, we have found out that underweight mothers are associated with increased risk of giving birth to LBW babies. This is consistent with other studies such as Han *et al.*, 2011[12] and Kanadys 2007.[13]

Our study has shown that macrosomia or babies with higher birth weight is common in obese and overweight women. Similar results were obtained with other studies such as Isaacs *et al.*;[14] Bianco *et al.,* 1998;[15] Cedergren, 2004.[16]

Low APGAR score and NICU admissions were more frequent in BMI Group 3, 4, and 5 patients. Scott-Pillai *et al.*, 2004,[7] also had similar results. Perinatal deaths were more common in underweight category because of LBW and severe perinatal asphyxia which is similar to study conducted by Cunningham and Teale, 2013.[17]

CONCLUSION

It can be concluded from our study that extremes of maternal BMI is associated with adverse maternal and perinatal outcome. While underweight was associated with anemia, nutritional deficiencies and LBW babies, obese and overweight was associated with gestational hypertension, PE, GDM, increased LSCS rate macrosomia and increased neonatal morbidity. Hence, adequate preconceptional counseling should be given to all women in reproductive age group so that they can attain normal BMI before conception. With proper management of pregnant women with abnormal BMI during antepartum, intrapartum, and postpartum period, by improving the awareness, and by increasing the accessibility to medical facilities, maternal and perinatal morbidity and mortality can be minimized.

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Original Article

Cytological Pattern of Cervical Smears in Leukorrhea

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Abstract

Introduction: Leukorrhea, one of the major problems in gynecological practice, can be "physiological" or "pathological." Common pathological causes are vaginitis, cervicitis, and cancers.

Purpose: To study the spectrum of cytological changes in leukorrhea according to The Bethesda System 2001; and to evaluate the role of cytology in early detection of cervical intraepithelial lesions and malignancies in patients of leukorrhea.

Materials and Methods: A total of 2544 cases were studied. Cervical scrape smears were taken and reported according to The Bethesda system, 2001.

Results: Out of 2544 cases, 2430 (95.52%) smears were adequate. A majority of 2216 (91.19%) were "Negative for intraepithelial lesion or malignancy" and 1402 (57.70%) smears revealed "Reactive cellular changes associated with inflammation" (RCCI). Specific infections were diagnosed in 392 (16.13%) smears. *Trichomonas vaginalis* was found to be the most common infectious agent 251 (10.33%) cases. 326 (13.41%) smears were "within normal limits." "Epithelial cell abnormalities" were detected in 212 (8.73%) smears. Of these, low-grade squamous intraepithelial lesion was most common 108 (4.44%). Atypical squamous cells of undetermined significance, high-grade squamous intraepithelial lesion, and squamous cell carcinoma were diagnosed in 6 (0.25%), 23 (0.94%), and 50 (2.06%) smears, respectively.

Conclusions: The Bethesda System of Classification, 2001, was found to be very useful. The most common finding in leukorrhea was RCCI. Infectious agents were identified in 16.13% cases and *T. vaginalis* was found to be the most common agent.Pap smear provided a simple and inexpensive tool for screening the patients of leukorrhea and helped in early institution of specific treatment.

Key words: Leukorrhea, Pap smear, The Bethesda System 2001

INTRODUCTION

One of the major problems in gynecological practice is "running of white substance in excess amounts" or leukorrhea. Its causes are physiological response, vaginitis, cervicitis, foreign bodies, or carcinoma. In Indian women poor genital hygiene is a major cause. Screening of all symptomatic women complaining of leukorrhea is necessary to detect cause and to pick up any cervical epithelial abnormalities, as precursor lesions of cancer cervix largely remain asymptomatic. Pap smear screening for cervical cancer and precancerous conditions has been proved to be very effective in cervical cancer prevention and in reducing mortality.[1] It is reliable and inexpensive.

Any diagnostic terminology should enable effective communication with the referring physician about the interpretation of the specimen. The report apart from being scientifically accurate should be easily understood by the treating physicians. The Bethesda System 2001 has clearly mentioned criteria and fixed terminologies making it easy for physician to understand and plan the treatment accordingly.[2]

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The objective of our study was to study the spectrum of cytological changes in leukorrhea according to The Bethesda System 2001 for reporting cervical cytology, and to evaluate the role of cytology in early detection of cervical squamous intraepithelial lesions and cervical malignancy in patients of leukorrhea.

MATERIALS AND METHODS

This study was carried out in a tertiary care institute over a period of 2 years. Total 2544 cases with complaint of leukorrhea were included, irrespective of their age.

Methods

With the patient in lithotomy position, a nonlubricated speculum was introduced in vagina to visualize the cervix. Longer portion of the bifid end of Ayre's spatula was inserted into the external os and rotated 360° maintaining firm pressure so that material is obtained from whole circumference of cervix. The spatula was withdrawn carefully without touching the vaginal wall and material was quickly spread on clean prelabeled slide in circular movements to cause uniform spreading of cells taking care that material from both sides of spatula was spread on the slide. The smear was fixed immediately within 10 s in 95% ethyl alcohol and fixed for a minimum of 30 min.

Smears were stained by the Papanicolaou method of staining.[3]

All smears were reported as per The Bethesda System 2001 for reporting cervical cytology which consists of four elements as follows:[2]

- Specimen type
- Specimen adequacy
- General categorization (optional)
- Interpretation/result.

RESULTS

In this study, according to parity, 58 cases (2.28%) were nullipara, 183 cases (7.19%) were para 1, 621 cases (24.41%) were para 2, and maximum cases 1682 (66.12%) were para 3 and above.

Of the total 2544 patients, maximum number of females 2106 (82.78%) had no other associated complaints apart from leukorrhea. 107 women (4.21%) complained of itching, 92 (3.63%) felt something coming out of vagina, 53 (2.08%) had lower backache, 47 (1.84%) had pain in abdomen, 42 (1.65%) had burning micturition, 38 (1.49%) with postmenopausal bleeding, 31 (1.22%) with postcoital bleeding, 28 women (1.10%) had associated bleeding per vaginam.

Table 1 shows age distribution of the cases in our study. Maximum cases (40.25%) were of 31-40 years of age and minimum cases (0.86%) were of <20 years age.

Out of 2544 smears, 2430 smears (95.52%) were satisfactory for evaluation and 114 smears (4.48%) were unsatisfactory.

Table 2 shows the general categorization of patients into negative for intraepithelial lesion malignancy (NILM), others and epithelial cell abnormalities. Table 3a and b shows complete categorization of smears into further subcategories according to The Bethesda System 2001.[2] A varied spectrum of organisms was seen in the cervical smears including some common ones like Bacterial vaginosis (Figure 1a), Trichomonas vaginalis (Figure 1b) and candida, and few less common organisms like Herpes Simplex Virus (Figure 1c), Actinomycetes and Microfilaria. We also encountered one case each of cysts of parasites, i.e. *Entamoeba histolytica* and *Enterobius vermicularis* which were later confirmed on stool examination of the respective patient.

DISCUSSION

Since the advent of Pap smear, the incidence of cervical cancers and also the mortality associated with it has greatly decreased due to widespread screening and early detection of epithelial abnormalities. Apart from cancer detection, Pap smear can also be used for detection of certain infections such as candida, trichomonas, herpes, HPV, and actinomycetes.

Table 1: Age distribution of cases

Age group (years)	Number of cases (%)
<20	22 (0.86)
21-30	789 (31.02)
31-40	1024 (40.25)
41-50	429 (16.86)
>50	280 (11.01)
Total	2544 (100.00)

Table 2: General categorization of smears according to The Bethesda System (2001)

General category	Number of smears (%)
NILM	2216 (91.19)
Other	02 (00.08)
Epithelial cell abnormality	212 (08.73)
Total	2430 (100.00)

NILM: Negative for intraepithelial lesion or malignancy

In this study, leukorrhea was the most common complaint among the women screened. Nikumbh *et al.*[4] and Misra *et al.*[5] also found leukorrhea to be the most common gynecological complaint. In our study, pruritus vulvae was the most common associated symptom along with leukorrhea while Panda *et al.*[6] found lower abdominal and lower back pain to be the most common associated symptom and pruritus vulvae the second common associated symptom.

Table 1 shows age distribution of the cases in our study. Maximum cases (40.25%) were of 31-40 years of age and minimum cases (0.86%) were of <20 years age. Nikumbh *et al.*[4] also found maximum cases (36.5%) to be in 31-40 years of age group. Similarly, Panda *et al.*[6] also found maximum cases (34%) of age group 31-35 years and minimum cases (4%) of age group 16-20 years.

It was noted that the majority of the women were multiparous, maximum (66.12%) being para 3 and above. Similarly, Nikumbh *et al.*[4] and Panda *et al.*[6] also noted maximum cases of para 3 and above, 48% and 71.78%, respectively.

In our study, adequacy was also fairly correlating with other studies. 95.52% smears were satisfactory in our study. Kapila *et al.*,[7] Misra *et al.*,[8] Mulay *et al.*,[9] and Wasti *et al.*[10] had 96.09%, 95.08%, 99.25%, and 99.75% satisfactory smears, respectively.

Table 2 shows general categorization of patients according to The Bethesda System 2001,[2] into NILM, others and epithelial cell abnormalities, out of which 91.19% were NILM and 8.73% had epithelial cell abnormalities. Similar results were obtained by Banik *et al.*,[11] where 91.81% were NILM and 8.19% had epithelial cell abnormalities. Other studies showed slightly less cases of epithelial cell abnormalities. Nikumbh *et al.*[4] found 94.20% NILM and 5.8% cases of epithelial cell abnormalities. Ghazal-Aswad *et al.*[12] and Ranabhat *et al.*[13] found 5% and 1.7% cases with epithelial cell abnormalities, respectively.

Table 3 shows complete categorization of smears into different categories according to The Bethesda System 2001. In our study, organisms were seen in 16.13% smears which were much higher than those of Nikumbh *et al.*[4] 1.93% and Mulay *et al.*[9] 6.05%.

Among organisms, trichomonas, and candida are the most consistently found organisms in other studies also. They are compared in Table 4.

Finding ova of parasites in cervical smears are also documented earlier in many studies. Martínez-Girón *et al.*[14] and Shetty *et al.*[15] encountered ova of *E. vermicularis* in cervical smears. Similarly, Walter.[16] has reported *Entamoeba* in cervical smears. Although the presence of these parasites is mostly due to contamination, it helps in diagnosis of the stool infection and starting specific therapy for it.

In our study, 61.65% smears were categorized as having "Other nonneoplastic findings." Whereas according to

Table 3a: Distribution of NILM smears into different categories as per The Bethesda System 2001

S. No.	Category (under NILM)	Number of cases (%)
1.	Normal	326 (13.41)
2.	Organisms	392 (16.13)
	Shift in flora suggestive of bacterial vaginosis	68 (2.80)
	Fungal organisms morphologically consistent with *Candida* spp.	45 (1.85)
	T. vaginalis	251 (10.33)
	Bacteria morphologically consistent with *Actinomyces* spp.	2 (0.08)
	Cellular changes consistent with herpes simplex virus	6 (0.25)
	Organisms morphologically consistent with *Leptothrix*	4 (0.16)
	Organism morphologically consistent with *Microfilaria*	1 (0.04)
	Organism morphologically consistent with *E. histolytica*	1 (0.04)
	Organism morphologically consistent with *E. vermicularis*	1 (0.04)
3.	Other nonneoplastic findings	1498 (61.65)
	Reactive cellular changes associated with	
	Inflammation (includes typical repair)	1402 (57.70)
	Radiation	8 (0.34)
	Intrauterine contraceptive device (IUD)	43 (1.76)
	Glandular cells status posthysterectomy	-
	Atrophy	45 (1.85)
	Total	2216 (91.19)

NILM: Negative for intraepithelial lesion or malignancy, *T. vaginalis: Trichomonas vaginalis, E. histolytica: Entamoeba histolytica, E. vermicularis: Enterobius vermicularis*

Table 3b: Distribution of smears with epithelial cell abnormalities into different categories according to The Bethesda System 2001

S. No.	Epithelial cell abnormality	Number of cases (%)
A.	Squamous cell abnormalities	
1.	ASCUS*	6 (0.25)
2.	ASC-H**	-
3.	LSIL***	108 (4.44)
4.	HSIL****	23 (0.94)
5.	Squamous cell carcinoma	50 (2.06)
B.	Glandular cell abnormalities	
1.	AGUS†	24 (0.99)
2.	Adenocarcinoma in situ	-
3.	Adenocarcinoma	1 (0.04)
	Total	212 (8.73)

*ASCUS: Atypical squamous cells of undetermined significance, **ASC-H: Atypical squamous cells cannot rule out high-grade lesion, ***LSIL: Low-grade squamous intraepithelial lesion, ****HSIL: High-grade squamous intraepithelial lesion, †AGUS: Atypical glandular cells of undetermined significance

Table 4: Comparison of prevalence of *Trichomonas* and *Candida* infection with other studies

Organism	Panda *et al.* (2013)	Nikumbh *et al.* (2012)	Mulay *et al.* (2009)	Wasti *et al.* (2004)	Misra *et al.* (1999)	Present study
Trichomonas (%)	6	0.98	0.35	0.61	3.1	10.33
Candida (%)	52	0.66	3.02	3.85	1.2	1.81

Table 5: Comparison of prevalence of epithelial cell abnormalities with other studies

???	Banik *et al.* (2011)	Balaha *et al.* (2011)	Nikumbh *et al.* (2012)	Mulay *et al.* (2009)	Kapila *et al.* (2006)	Present study
ASCUS* (%)	0.18	2.99	0.96	0.64	2.2	0.25
ASC-H** (%)	-	0.6	-	-	-	0
LSIL*** (%)	6.36	0.09	0.96	0.216	1	4.44
HSIL† (%)	1.18	0.68	1.98	0.16	0.2	0.94
SCC†† (%)		0.34	1.6		0.05	2.06
AGUS††† (%)	0.12	0.09	0.4	0.316	0.8	0.99
Adenocarcinoma		-	0		-	0.04

*ASCUS: Atypical squamous cells of undetermined significance, **ASC-H: Atypical squamous cells cannot rule out high-grade lesion, ***LSIL: Low-grade squamous intraepithelial lesion, †HSIL: High grade squamous intraepithelial lesion, ††SCC: Squamous cell carcinoma, †††AGUS: Atypical glandular cells of undetermined significance

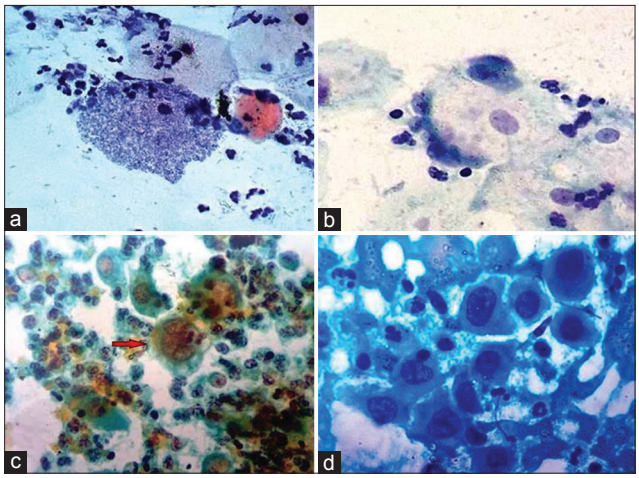

Figure 1: (a) Clue cell; (b) *Trichomonas vaginalis*, sticking to the edges of the squamous cell; (c) cellular changes of herpes simplex virus showing multinucleation, intranuclear inclusions, nuclear molding and margination of chromatin; (d) high-grade squamous intraepithelial lesion

Nikumbh *et al.*[4] and Mulay *et al.*,[9] 92.36% and 43.02%, respectively, showed "Other nonneoplastic findings."

Reactive cellular changes of inflammation or nonspecific inflammation were present in 57.70% smears in our study which was similar to findings of Wasti *et al.*[10] as 59.3%. Nikumbh *et al.*,[4] and Mulay *et al.*[9] had different findings from ours, 86.19% and 19.61%, respectively.

1.85% smears showed changes of atrophy in our study. Similarly, Balaha *et al.*[17] and Nikumbh *et al.*[4] found 0.34% and 3.29% of cases with changes of atrophy which correlates with our results.

Epithelial cell abnormalities were also further classified as given in Table 3b. A comparison of our study with other studies is shown in Table 5.

CONCLUSION

The Bethesda System 2001 was found to be a very useful diagnostic tool as well as for classification and reporting of cervical smears. The most common cause of leukorrhea was "Reactive cellular changes associated with inflammation" in 57.70%. Infectious agents were identified in 16.13% among which *T. vaginalis* was found to be the most common. Cervical "epithelial cell abnormalities" were diagnosed in 8.73% cases of leukorrhea and their prevalence correlated with increasing parity.

Pap smear provided a simple and inexpensive tool for screening the patients of leukorrhea. Early detection of "Epithelial Cell Abnormalities" and various common as well as uncommon infections helped in early institution of specific treatment, and thus reducing the risk of progression of dysplasia to malignancies.

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Original Article

Clinical and Social Determinants of Duration of Untreated Psychoses

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Abstract

Introduction: Outcome of schizophrenia has been repeatedly demonstrated to be "good" and "favorable," which generally implies that most of the patients treated adequately are able to maintain a reasonable quality of life, remain free from distressing symptoms, can function at a moderate level and live a life outside psychiatric institutions in the community.

Aim: To study clinical and social determinants of duration of untreated psychoses in drug naïve schizophrenic patients.

Methods: 100 consecutive patients diagnosed and admitted as inpatient schizophrenia in institute of mental health, Madras Medical College Hospital. Study variables include scales scale for assessment of positive symptoms (SAPS), scale for assessment of negative symptoms (SANS), CGI-SCH, and global assessment of functioning were given and age criteria 18-45 years, drug naïve patients and patients with a diagnosis of schizophrenia.

Results: A total of 100 patients were selected for the study of which 97 was obtained assessed at baseline with SAPS and SANS for psychopathology, PSA scale to assess premorbid functioning, duration of untreated psychosis and a sociodemographic profile were obtained, 63 patients were assessed at 8 weeks of follow-up for psychopathology.

Conclusion: Longer duration of untreated psychoses is associated with higher age at presentation, higher negative symptoms, and poor premorbid functioning. Improved patients have a shorter duration of untreated psychoses and better premorbid functioning than unimproved patients.

Key words: Duration of untreated psychosis, Psychopathology, Schizophrenia

INTRODUCTION

A large number of studies have examined the prognostic value of premorbid sociodemographic and psychopathological factors on outcome in schizophrenia.[1-3] More recently several groups of investigators have proposed that a long duration of untreated psychosis (DUP) initially may also affect long-term outcome in schizophrenia.[4] A recent meta-analysis of the more methodologically robust studies of duration of untreated psychoses and outcomes by Marshall *et al.* suggests there is a modest association between duration of untreated psychoses and outcomes and that this holds independently of premorbid adjustment.[5] Using data collected as part of study of first onset psychoses we sought to investigate the relationship between DUP and both clinical and social variables, specifically, we sought to test the hypotheses that there is no significant association of duration of untreated psychoses and type of family and mode of onset or socioeconomic status or age and gender.

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METHODS

A total of 100 consecutive patients admitted as inpatients in the institute of mental health, fulfilling the ICD-10 criteria for schizophrenia and who were never treated outside were included in the study age group was within 18-45 years and drug naïve patients with reliable informants. After complete description of study, written informed consent was obtained from the participants. Exclusion criteria were

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patients under age of 18 years or above 45 years, and a history of head injury, evidence of psychotic symptoms precipitated by an organic cause; previous treatment for psychosis; transient psychotic symptoms resulting from acute intoxication as defined by ICD-10.

Data relating to date of onset of psychosis were collated from interviews with the patient and a close relative of the patient. We asked when the patient first experienced or when the family members first noticed psychotic symptoms DUP was defined as the period in weeks from the onset of psychosis to first contact with statutory mental health services. In line with previous studies (Craig *et al*., 2000 and Morgan *et al*., 2006) onset of psychosis was defined as the presence for 1 week or more of one of the following psychotic symptoms: Delusions; hallucinations; marked thought disorder; marked psychomotor disorder; bizarre, grossly inappropriate and/or disorganized behavior with a marked deterioration in function. A rating of onset was made only when there was a clear, unequivocal description from any source of symptoms meeting these criteria. In this study, the end point was considered as admission to the hospital. Our end-point, therefore, was contact with mental health services. Schizophrenia was diagnosed as per ICD-10 criteria for schizophrenia.

RESULTS

During our study period, 100 consecutive patients were screened, evaluated, and entered into the study out of which 3 patients were excluded, one patient was found to be HIV positive and 20 patients were found missing from ward. 97 patients were available at baseline assessment was done.

The correlation of log DUP with psychotic and disorganized symptom domain was nonsignificant ($P > 0.05$). There is a significant correlation between DUP and negative symptoms domain at baseline presentation ($P < 0.05$) (Table 1).

Among the improved group of patients, 58.5% were paranoid subtype, 2.4% were hebephrenic type, 2.4% were catatonic type, and 36.6% were of undifferentiated subtype. In the unimproved group, 36.4% were paranoid type, 4.5% were hebephrenic type, and 59.1% were of undifferentiated subtype the difference was not statistically significant (Table 2). Among the improved group, 12.2% were uneducated, 24.4% were educated up to primary level and 29.3% update secondary level. The difference was not statistically significant (Table 3).

Among the improved group of patients, 51.2% were males and 48.8% were females. In the unimproved group, 50% were males and 50% were females, the difference was not statistically significant (Table 4).

In the improved group, 82.9% were from lower socioeconomic group, 14.7% were from middle socioeconomic group, and 2.4% belonged to higher socioeconomic group in the unimproved group 72.7% were from the lower socioeconomic group, 22.8% were from the middle socioeconomic group, and 4.5% belonged to higher socioeconomic group the difference was not statistically significant. As our study was done at a government institute, majority of the individual were from the lower socioeconomic classes (Table 5).

Table 1: Clinical variables of DUP

Log DUP	Correlation coefficient	*P* value
Psychotic domain	0.021	0.838
Disorganized	0.192	0.061
Negative	0.256	0.011
Premorbid social adjustment score	0.334	0.001

DUP: Duration of untreated psychosis

Table 2: Comparison of groups by diagnosis

Diagnosis	Improved (%)	Unimproved (%)	Total	*P* value
	n (58.5)	*n* (36.4)		
Paranoid	24 (2.4)	8 (4.5)	32	0.281
Hebephrenic	1 (2.4)	1	2	
Catatonic	1 (36.6)	0 (59.1)	1	
Undifferentiated	15 (100)	13 (100)	28	
Total	41	22	63	

Table 3: Social variables of DUP

Education	Improved (%)	Unimproved (%)	Total	P value
Uneducated	5 (12.2)	3 (13.6)	8	0.401
Primary	10 (24.4)	7 (31.8)	17	
Secondary	12 (29.3)	6 (27.3)	18	
High school	3 (7.3)	4 (18.2)	7	
Graduate	11 (26.8)	2 (9.1)	3	

DUP: Duration of untreated psychosis

Table 4: Gender wise distribution of DUP

Gender	*n* (%)		Total	*P* value
	Improved	Unimproved		
Male	21 (51.2)	11 (50.0)	32	0.092
Female	20 (48.8)	11 (50.0)	31	
Total	63 (100)	22 (100)	63	

DUP: Duration of untreated psychosis

Table 5: Sociodemographic variables and DUP

Socioeconomic	*n* (%)		Total	*P* value
	Improved	Unimproved		
Status				
Low	34 (82.9)	16 (72.7)	50	0.591
Middle	6 (14.7)	5 (22.8)	11	
High	1 (2.4)	1 (4.5)	2	
Total	41 (100)	22 (100)	63	

DUP: Duration of untreated psychosis

DISCUSSION

There is no significant association between the subtypes of schizophrenia with the duration of untreated psychoses at baseline assessment only few studies have studied the relation of diagnostic subtypes with DUP and have not found any significant association. In our study, premorbid functioning is found to have a positive correlation with duration of untreated psychoses, showing that poor premorbid functioning is associated with a longer DUP than those with a better premorbid functioning, this finding is similar to the studies done by Verdoux *et al*.[6] The correlation of DUP with symptom severity at baseline in this study has found a significant positive correlation with negative symptoms, but not with the disorganization and psychotic symptom domain. This finding is similar to the studies that have found a longer DUP to be associated with higher levels of negative or deficit symptoms at first presentation.[7] The negative correlation of DUP with psychotic symptoms domain in the study, though not significant implies that schizophrenic patients with positive symptoms seek treatment earlier and hence have a shorter duration of untreated psychoses. Drake *et al*. reported that longer DUP was associated with higher positive symptoms at presentation which is not found in our study. Some of the studies do not find any such association between DUP and baseline symptoms.[8-10] The total number of patients at 8 weeks assessment dips 63 (65%) and the follow-up rate is considerably lower when compared to most other studies, both Indian and studies done in western countries. The poor attrition rate could not be explained by any of the sociodemographic and clinical variables and the duration of untreated psychoses, a finding similar to the study done by Harrigan *et al*.,[10] where they compared between those who completed follow-up and those who did not. Information regarding the reasons for dropout was not available as those patients and their relatives could not be traced by any means.

The role of sociodemographic variables in determining the duration of untreated psychoses has given contrasting results across various studies. Studies have shown that males have a longer DUP than females but we could not establish any such difference in gender to be associated with DUP. Numerous studies have not reported any relation of DUP with gender.

The finding of a significant positive correlation of DUP with the age at first presentation shows that the duration of untreated psychoses increases as the age at first presentation to treatment increases. The result being similar to the findings of Padmavathi *et al*.[2] that never treated patients were older in age and ill for a longer duration and were more symptomatic and severely disabled. This finding is in contrary to other studies that have not found a. association between age and DUP.

There is no significant correlation of duration of untreated psychoses with the educational level, marital status, and socioeconomic status at baseline assessment, a finding which is similar to most other studies. One study in India has reported that untreated patients were most often uneducated and divorced and such a finding is not found in our study. In our study, we found no correlation between DUP and employment. A finding contrary to the report of Morgan *et al*.[11] that unemployment has a less strong effect on duration of untreated psychoses.

Some of the Indian studies have reported that a longer duration of untreated illness in schizophrenic patients was due to the larger extended joint family, which was able to compensate and cope with the dysfunctional member, concluding that such family system seemed to be a crucial factor related to the delay in treatment. In our study, although 70% of the patients were in the joint family system, there was no significant correlation of family type with DUP, in the West London first episode study of schizophrenia most of the patients were living alone or homeless. However, this study carried out in a government institute has its limitations regarding demographic variables such as educational status, socioeconomic status, and employment.

CONCLUSION

The findings from this study suggest that a longer duration of untreated psychoses is associated with increased age at presentation, higher negative symptoms, and poor premorbid functioning; it also shows that improved patients have a shorter duration of untreated psychoses and better premorbid functioning than the unimproved patients but the association is not significant after the confounding factors were controlled. This study concludes that duration of untreated psychoses is not an independent predictor of outcome as stated in literature. It is conceivable that the reported better outcome for schizophrenia in India is unlikely to be because of shorter DUP.

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Original Article

Skeletal Stability of Cleft Maxilla in Le-Fort-I Maxillary Advancement

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Abstract

Introduction: To provide good esthetics and function in patients with cleft associated midface deformity, the field of oral and maxillofacial surgery offers methods of operation that leads to near normal status. The usual method of correcting the deformity is midface osteotomies (Le-Fort-I, High Le-Fort-I, Le-Fort-II, and Le-Fort-III) with advancement of maxilla. However, these surgeries are prone for relapse which is an annoying problem, irrespective of using semi-rigid fixation techniques.

Materials and Methods: Five patients who were reported to the department with cleft associated midface deformity. All were females with mean age of 21.6 years (range 17-28 years). All the patients underwent conventional Le-Fort-I osteotomy advancement and fixation with "L" shaped stainless steel miniplates. The skeletal and dental stability were evaluated through clinical presentation and serial lateral cephalograms (pre-operative, immediate post-operative, and 6-month post-operative).

Results: The outcome of the surgery was found to be satisfactory with minimal relapse of 11%. However, a longer follow-up is essential to consolidate our findings.

Conclusion: Correcting the deformities of cleft lip and palate patients with severe maxillary hypoplasia presents a definite challenge for oral and maxillofacial surgeon. In this study, all the patients underwent Le-Fort-I osteotomy and fixation with "L" shaped miniplates having favorable stability, and the outcome of the surgery was found to be satisfactory with minimal relapse of 11%.

Key words: Cleft lip and palate, Le-Fort-I osteotomy, Maxillary hypoplasia, Stability

INTRODUCTION

Literature regarding congenital anomalies of lip and palate exists since prehistoric time. Some form of cleft lip and cleft palate occurs in one out of every 800 live births. These deformities of children produce anxiety to their parents, as their children suffer from difficulty in feeding, impairment in speech, unacceptable appearance, and improper occlusion. To provide good esthetics and function in patients with cleft associated midface deformity, the field of oral and maxillofacial surgery offers methods of operation that leads to near normal status. The usual method of correcting the deformity is midface osteotomies (Le-Fort-I, High Le-Fort-I, Le-Fort-II, and Le-Fort-III) with advancement of maxilla. In many patients, a combination of simultaneous setback of mandible or segmental osteotomies is necessary for rehabilitation.

However, these surgeries are prone for relapse which is an annoying problem. Literature shows relapse is more likely to occur in cleft patients than in non-cleft patients with maxillary hypoplasia, irrespective of using semi-rigid fixation techniques. The purpose of this study is an attempt to evaluate skeletal stability pattern of traditional cleft Le-Fort-I osteotomy in the management of midface hypoplasia secondary to cleft lip and palate deformity.

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MATERIALS AND METHODS

This study was undertaken on five patients who reported to the department with cleft associated midface deformity. All were females with mean age of 21.6 years (range 17-28 years). All the patients had primary surgery (lip correction at

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average age of 8 months, palatal correction at the average age of 14 months). Out of five patients two patients had previous alveolar bone grafting. All the patients were having well-aligned dental arch with previous orthodontic treatment. All the patients underwent conventional Le-Fort-I osteotomy advancement and fixation with "L" shaped stainless steel miniplates (1.5 mm - 4 hole with bar) and post-operative intermaxillary fixation for 4 weeks followed by functional elastics for 2 weeks. One patient had interpositional corticocancellous bone graft. The graft was taken from iliac crest. The skeletal and dental stability of the procedure were evaluated through clinical presentation and serial lateral cephalograms (pre-operative, immediate post-operative, and 6 months post-operative).

Evaluation of Skeletal Stability

The skeletal stability after surgery was evaluated by serial lateral cephalometric radiographs taken preoperatively, immediate postoperatively, and 6 months postoperatively. The Quejada method of analysis was used described by Cheung *et al.*[1] A line was drawn from sella to nasion (SN line) and horizontal plane was taken at 7° from SN. The landmarks used were point of maxilla, upper incisal tip, the distal cusp of the upper last molar, and the upper incisor to SN angulation. All the cephalographs were taken using the same machine (Figure 1).

The radiographs of each patient were traced at the same time. Movement of the selected landmarks in the horizontal and vertical plane was determined in relation to a perpendicular line taken from the horizontal plane. The surgical movement was determined by measuring the difference between the first post-operative radiograph and the pre-operative one. The total post-surgical relapse was determined by measuring the difference between latest post-operative radiograph and immediate post-operative radiograph.

OBSERVATION AND RESULTS

All the patients were postoperatively observed and followed for a minimum period of 6-month. Periodic photographs and cephalograms were also obtained. The parameters used for evaluation are stability of both skeletal and dental (Table 1 and Figures 2 and 3).

DISCUSSION

The common developmental disturbance of the facial skeleton associated with cleft lip and palate is maxillary hypoplasia. Bishara[2] evaluated the facial growth in operated and nonoperated individuals with isolated cleft of the palate and concluded that the growth of maxilla is impaired in operated patients. Bishara *et al.*,[3] the disproportionate jaw growth is mainly due to inherent cleft defect and previous surgical intervention for primary defect. Essentially, all the patients with cleft defects will be associated with severe malocclusion. To get esthetic harmony and effective mastication these patients require midface osteotomy, usually Le-Fort-I with advancement of maxillary segments.

Traditionally, maxillomandibular disparities in patients with clefts were compensated with the use of prosthetic devices or through surgical retropositioning of the mandible.[4] The history of horizontal maxillary osteotomy (Le-Fort-I) has been reviewed by Drommer,[5] and he chronicles developments in this area, beginning in 1859 with von Langenbeck, who used a horizontal sectioning of the maxilla. Axhausen,[6] in 1934, published the first report of horizontal sectioning of the maxilla to correct midface deformity associated with cleft lip and cleft palate.

Primary stability of repositioned skeletal parts is desirable to prevent relapse. According to Luyk and Ward-Booth,[7] the major cause of instability is the lack of adequate fixation of osteotomized segment. Mini bone plates have been suggested in the past for stabilization of Le-Fort-I osteotomies as quoted by Luyk and Ward-Booth[7] as their use increasing the area of contact for fixation, as quoted by Drommer and Luhr[8] the first author who used miniplates in cleft osteotomy is Horster in 1980. Eskenazi and Schendel[9] confirmed the superiority of miniplates in reducing the relapse in both the horizontal and vertical planes. The direct skeletal fixation is supplemented by intermaxillary fixation for variable period to achieve maximum stability.[7,10,11]

Multiple factors are considered to be related to relapse after maxillary advancement in cleft patients.[12] Scarring from previous surgery, timing of surgery, type of cleft and presence of pharyngeal flap, mobilization of osteotomized

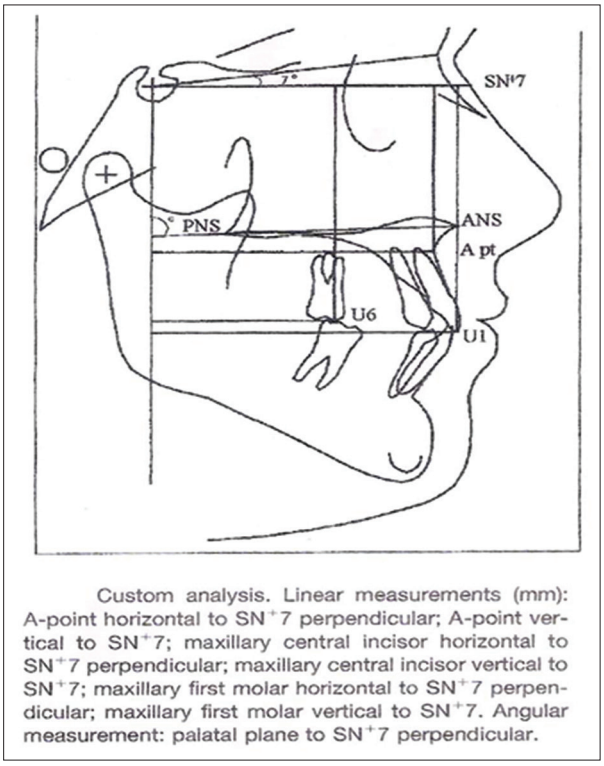
Table 1: Master chart

Patient no	HA immediate (in mm)	HA 6 months (in mm)	HA relapse In 6 months (in mm)	VD immediate (in mm)	VD 6 months (in mm)	VD relapse (in mm)
1	9	8	1	4	3	1
2	4	4	0	2	2	0
3	6	5	1	3	2	1
4	7	6	1	3	3	0
5	4	4	0	5	4	1

HA: Horizontal advancement, VD: Vertical dimension

segment intraoperatively, amount of advancement and use of interpositional bone grafting, fixation technique of osteotomized segment, and achieving proper occlusion intraoperatively.

The inherent palatal scar and its resistance to any large transposition movement probably contributes to the large relapse percentage of up to 25% in both horizontal and vertical planes in cleft patients.[13] The amount of relapse can be reduced by pre-operative orthodontics to align the arch and level the teeth, sufficient mobilization of osteotomized segment intraoperatively,[14] use of interpositional bone graft when the amount of advancement is more than 6 mm,[7] use of miniplates for fixation of osteotomized segment.[9]



Custom analysis. Linear measurements (mm): A-point horizontal to SN$^+$7 perpendicular; A-point vertical to SN$^+$7; maxillary central incisor horizontal to SN$^+$7 perpendicular; maxillary central incisor vertical to SN$^+$7; maxillary first molar horizontal to SN$^+$7 perpendicular; maxillary first molar vertical to SN$^+$7. Angular measurement: palatal plane to SN$^+$7 perpendicular.

Figure 1: Skeletal stability evaluation

In our study, all the patients were underwent orthodontic treatment pre surgically. In the pre-operative work up (plan), post-operative occlusion was determined through model study (mock positioning), and the same prediction was achieved peroperatively. Intraoperatively, the osteotomized segment was mobilized sufficiently. A mobilization splint was fabricated and used to protect the soft and hard tissues while the osteotomized maxilla was repositioned. In one patient, we used interpositional bone graft as the amount of advancement was larger (9 mm). As the proper occlusion has a role in reducing the relapse, importance was given to achieve positive overbite of the anteriors and proper intercuspation of posteriors in all our cases intraoperatively. "L" shaped stainless steel miniplates were used for fixation of the fragment in all patients.

The results of our study are comparable to others study, and we had minimal amount of skeletal relapse in three patients (11%), and two patients maintained the initial 4 mm of advancement with the follow-up of 6-month.

CONCLUSION

Treatment planning and surgery are generally more complex for cleft lip and palate patients than noncleft patients. We have conducted a prospective study which comprised five female patients, who had undergone primary lip and palate repair elsewhere. All these patients underwent Le-Fort-I osteotomy and fixation with "L" shaped miniplates. The results were analyzed using lateral cephalograms taken before surgery, immediate post surgically, and 6 months postoperatively. The outcome of the surgery was found to

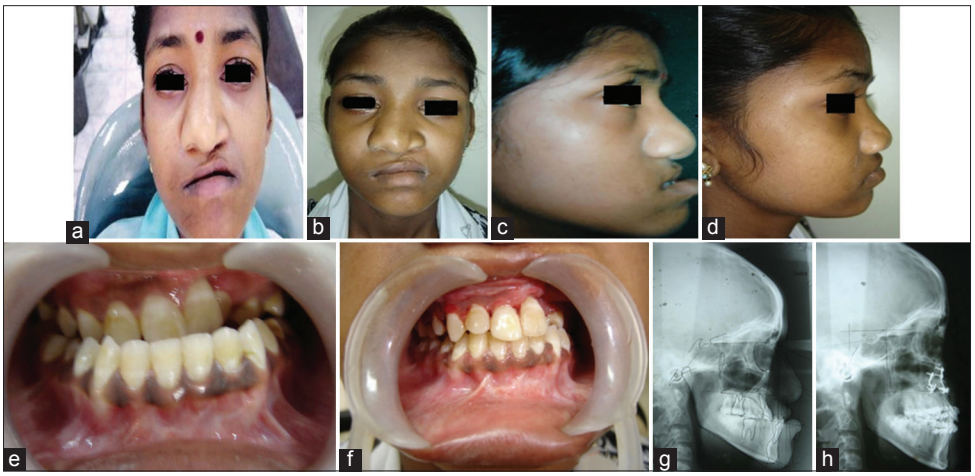


Figure 2: Case 1 - (a) Pre-operative frontal view, (b) post-operative frontal view, (c) pre-operative lateral view, (d) post-operative lateral view, (e) pre-operative occlusal view, (f) post-operative occlusal view, (g) pre-operative lateral cephalograms, (h) post-operative lateral cephalograms

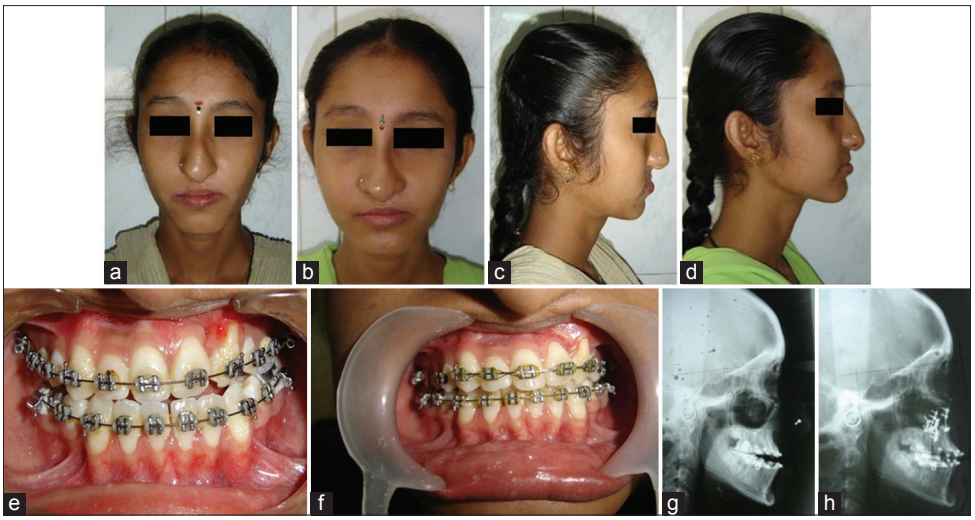


Figure 3: Case - 2 (a) Pre-operative frontal view, (b) post-operative frontal view, (c) pre-operative lateral view, (d) post-operative lateral view, (e) pre-operative occlusal view, (f) post-operative occlusal view, (g) pre-operative lateral cephalogram, (h) post-operative lateral cephalogram

be satisfactory with minimal relapse of 11% for patients with larger magnitude of advancement (more than 6 mm) and nil relapse for patients with lesser magnitude of advancement (<5 mm). However, a longer follow-up is essential to consolidate our findings, considering the smaller sample size and shorter follow-up.

To conclude, whenever a Le-Fort-I advancement of the maxilla is planned for cleft patients, they should be considered distinct from the noncleft patients in view of the incision designing, mobilization of osteotomized segment, magnitude of advancement, and fixation techniques. A carefully designed flap, radical mobilization of osteotomized segment with the use of interposition bone grafts in larger movements, achieving a positive overbite and proper intercuspation peroperatively and fixation with miniplates will offer better skeletal stability in cleft patients.

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Original Article

Teratomas of Head and Neck: An Observational Study

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Abstract

Background: Epidermoids are ectoderm lined inclusion cysts which can be present anywhere in the body, but are rare in head and neck.

Objectives: Although only 7% of the epidermoid cysts occur in head and neck region they are a part of differential diagnosis of neck swellings.

Materials and Methods: Cases which were proven as dermoid or epidermoid cysts by FNAC or by histopathology.

Observation: Male patients were more affected than female patients.

Conclusion: Complete removal should be carried out to prevent recurrence.

Key words: Teratoma, Dermoid cysts, Epidermoid cysts, Head and neck, Oropharynx

INTRODUCTION

Dermoids and epidermoids are ectoderm lined inclusion cysts that differ in complexity. Epidermoids contain squamous epithelium only whereas dermoids contain hair, sebaceous and sweat glands along with squamous epithelium. Both arise from trapped pouches of ectoderm, near normal folds or from failure of surface ectoderm to separate from the neural tube. These slowly expanding, unilocular cystic masses usually produce mild symptoms.[1] Dermoids consists of several parenchymal cells arising from ectoderm, mesoderm, and endoderm. Only 7% of them occur in head and neck region.[2] They commonly occur in the orbit, calvarial diploic space and intracranially.[1] They are rarer in oropharynx.[3] In this study, we present a series of dermoid and epidermoid cysts who presented to our institution over a period of 1 year.

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MATERIALS AND METHODS

This was an observational study carried out in the department of otorhinolaryngology, Sri Siddhartha Medical College, Tumkur, Karnataka from January 2016 to December 2016. A total of 60 patients of the 3432 outpatients were included. In the same period, 500 cases of dermoid and epidermoid cysts were diagnosed in various departments of our institution.

Patients aged more than 16 years who presented with longstanding swelling in the head and neck region, which were proven as dermoid or epidermoid cyst either by FNAC or histopathological examination were included in the study.

The selected patients were subjected to detailed history followed by complete clinical examination. All patients underwent either ultrasonography or computed tomography over the region of the swelling. They also underwent FNAC of the swelling and the diagnosis of dermoid or epidermoid cyst was made. Patients later underwent surgical excision and the diagnosis was confirmed by histopathology.

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Procedures

Patients with postaural epidermoid cysts underwent excision of the lesion through postaural approach (Wilde's incision) under local anesthesia with sedation. Patients with epidermoid cyst in the parotid region and preauricular region underwent excision through standard parotidectomy approach. In case of epidermoid cyst over the maxilla, sublabial approach was followed. In case of epidermoid cyst over forehead and posterior triangle an elliptical incision was made and the cyst was dissected. In case of oropharyngeal dermoid tonsillectomy was performed along with cyst excision.

RESULTS

In this study, the age of patients varied between 20 years and 60 years. They were no patients who were above 61 years (Table 1).

In this series, three groups had 2 patients each. There was no patient belonging to the age group of 41-50 years.

The age group of outpatients during that period was as follows (Table 2).

The chi-square test done shows the difference between the age group prevalence is not significant.

Sex Distribution

In this series, there were 50 male patients and 10 female patients (Table 3).

Sex distribution among our outpatients was as follows (Table 4).

Site Distribution

In this series, there were 25 patients with epidermoid cysts in the postauricular region, 10 patients in the parotid region, 10 in the preauricular, 5 over the maxilla and fore head, 4 in the posterior triangle and 1 in the oropharynx (Table 5).

Table 1: Age group of teratoma patients

Age group	Number of cases (%)
21-30	15 (25)
31-40	20 (33.3)
41-50	10 (16.7)
51-60	15 (25)

Table 2: Age group of out patients

Age group	Number of outpatients	Percentage	Number of cases
21-30	549	16	15
31-40	755	22	20
41-50	961	28	10
51-60	412	12	15
61<	755	22	Nil

Table 3: Sex distribution of teratoma patients

Sex	Number of cases (%)
Males	50 (83.3)
Females	10 (16.7)

Table 4: Sex distribution of out patients

Sex	Number of outpatients	Percentage	Number of cases
Males	1842	53.7	50
Females	1590	46.3	10

Table 5: Site distribution

Site	Number of cases (%)
Postauricular	25 (41.7)
Parotid	10 (16.7)
Preauricular	10 (16.7)
Over the maxilla	5 (8.3)
Posterior triangle	4 (6.7)
Fore head	5 (8.3)
Oropharynx	1 (1.67)

DISCUSSION

Epidermoids are derived from ectoderm, but they are inclusion cysts that are lined only by squamous epithelium. A dermoid is also an ectodermal inclusion cyst, but it contains more complex tissues which are also derived from ectoderm.[1] Teratoma is derived from the Greek word "teraton" meaning monster. Teratoma need not necessarily contain tissues derived from all three germ layers.[3] A teratoma can be defined as a true neoplasm that contains tissues that are either foreign to the primary site of origin or histologically diverse and represent more than one of the embryonic germ layers. The designation of teratoma may be appropriate even for a lesion with tissues derived from a single embryonic germ layer, if the tumor shows histologically divergent differentiation. Such teratomas can be found in the head and neck and can be purely ectodermal.[1] Teratomas are of four types. Dermoids that are composed of both ectoderm and mesoderm. Teratoid tumors are composed of all three germ layers but are poorly differentiated. True teratomas where all germ layers are well differentiated into specific tissues. Epignathi are limb-like structures protruding from the mouth and present the highest form of teratoma differentiation in which fetal organs have developed.[3]

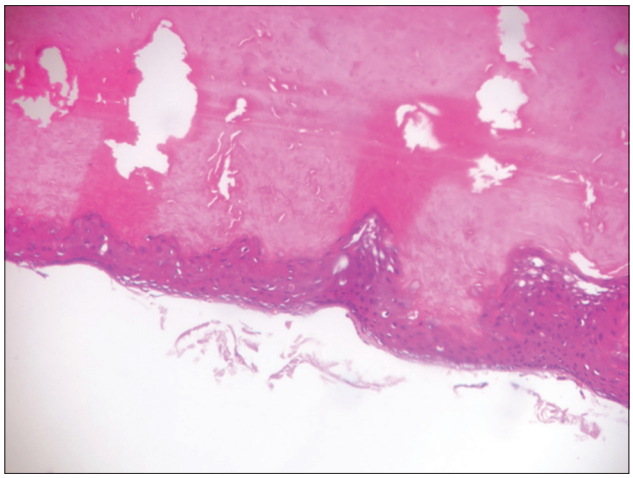

Figure 1: Histopathological examination under 40X magnification

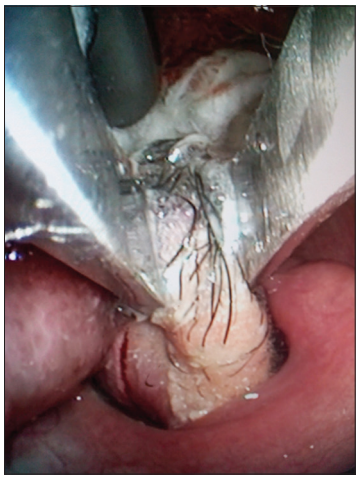

Figure 2: Tonsillectomy

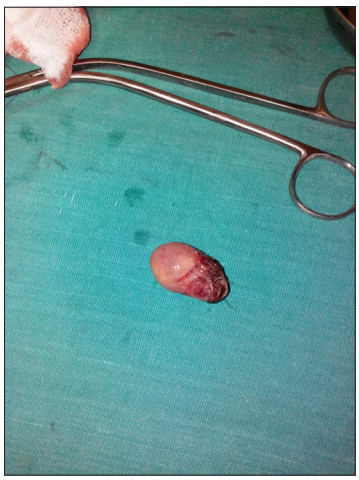

Figure 3: Gross specimen

Epidermoid cysts can be of congenital or acquired type. Congenital type is due to entrapment of ectodermal substance between the midline fusion of first and second branchial arches during third and fourth intrauterine life. Acquired type cysts usually occur because of infection around pilosebaceous follicle and sometime deep implantation of epidermis due to penetrating or blunt injury. It is a slow growing and nontender mass. When it is present in dermis, it can raise epidermis to produce a firm elastic dome-shaped protuberance which is mobile over the deeper structures. They grow slowly and may become inflamed and firm gradually. Suppuration may occur.[2]

Manoharan *et al.* reported postauricular sinuses are the most common etiology for recurrent postaural abscess followed by dermoid cyst.[3] Ravindranath *et al.* reported epidermoid cyst to be most common in the lateral side of the neck and gingiva followed by the forehead region.[4] Dhabholkar *et al.* reported 3 cases of dermoid cysts out of which 2 were located in the floor of the mouth and another in the midline of the neck.[6] Ultrasonography is the best investigation for these types of cyst. It is economical, reliable, and without radiation exposure. Surgical excision of the cyst is often required and the entire cyst wall is removed to prevent recurrence. Incomplete removal is common if attempted in the presence of recent infection.[2]

CONCLUSION

Although only 7% of the dermoid and epidermoid cysts occur in head and neck, they form an important differential diagnosis of head and neck swellings among adults. A unilateral tonsillar enlargement is often considered as Quinsy, tonsillar cyst or malignancy, but congenital teratoma should be considered as a differential diagnosis. Surgical excision is required and histopathological examination should be mandatory. Complete removal must be carried out to prevent recurrence.

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Original Article

Knowledge and Vaccination Coverage of Hepatitis-B among 1st Year MBBS Students at Indira Gandhi Institute of Medical Sciences, Patna

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Abstract

Introduction: According to the World Health Organization hepatitis-B is the world's most common liver infection, which is caused by a DNA-virus. The lifespan chance of problems such as chronic hepatitis, cirrhosis, and hepatocellular carcinoma with chronic hepatitis-B virus infection is a vital concern for health-care personnel.

Aim: This study was conducted to assess the current knowledge and vaccination coverage for hepatitis-B among 1st year MBBS students.

Materials and Methods: A cross-sectional study was organized in the year 2016 on 100 MBBS students of the Indira Gandhi Institute of Medical Sciences (IGIMS), Patna. A semi-structured questionnaire was use to collect information. The data were examined in the form of percentage and fraction, and the Chi-square test was applied.

Results: A majority (81.6%) of MBBS students showed a good level of knowledge regarding hepatitis-B infection. The correct knowledge regarding postexposure prophylaxis and mode of transmission of hepatitis-B were 74% and 92%, respectively. It was found that 90% of the respondents correctly mentioned the mode of transmission and vaccination as a measure of prevention of hepatitis-B, 64% among all students were fully vaccinated against hepatitis-B. However, in a number of subjects, there is a lack of knowledge about prophylaxis, vaccination, and the treatment of hepatitis-B.

Conclusion: There is a crucial need for health education to improve the knowledge of pre MBBS course toward hepatitis-B infection.

Key words: Hepatitis-B infection, Knowledge, MBBS students, Vaccination coverage

INTRODUCTION

According to the World Health Organization (WHO) hepatitis-B is the world's most common liver infection. The virus is highly infectious, 50-100 times more than human immunodeficiency virus (HIV), and is transmitted through blood, semen, vaginal secretion, and mucous membranes. There are more than 2 billion people Worldwide having recent or previous hepatitis-B infection and 350 million are chronic carriers.[1] In South East Asian Region, there is approximately 80 million hepatitis-B virus (HBV) carriers (about 6% of the total population).[2] The most common route of transmission is unsafe sex, high-risk blood transfusions,contaminated needles, from mother to child at birth, close domiciliary touch and between children in early infant. HBV is specific to other sexually transmitted disease it can be preventable with vaccine.[1]

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The infection heals in adults and they become healthy, but 90% in newborn and 30-50% in young children, the infection takes a path to chronic hepatitis-B.[1] This provides an increased risk, approximately 25% that they subsequent in life will suffer from liver cirrhosis and/or carcinoma of liver, if the infection is not medically treated.[1,3] HBV is quickly transmitted by percutaneous or mucous

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membrane as the HIV, although, HBV has 50-100 times more infection rate (WHO, 2012). HBV infection has been determined as an important occupational hazard for health-care workers.[1] Transmission of infection is unusual between the persons who have been immunized but it may be as high as 30% among those who are not vaccinated.[4] Moreover, in an estimate 15-40% of chronic HBV transporter were susceptible to develop liver cirrhosis and hepatocellular carcinoma.[5] HBV is a challenging ailment that results in 0.6 million deaths yearly. Although HBV is modified as "disease of priority," there is a persistent increase in detection of new cases worldwide. HBV is common in the Asia Pacific region and 10-15 million people suffer from this disease.[6-8] The spread of HBV chronic infection is particularly high in Sub-Saharan Africa, ranging from 7% to 26%.[9] The objective of the study was to assess the knowledge and vaccination coverage on hepatitis-B among 1st year MBBS students studying at Indira Gandhi Institute of Medical Sciences (IGIMS) Medical College, Patna.

MATERIALS AND METHODS

A cross-sectional study was carried out among 1st year MBBS students studying at IGIMS and Medical College, Patna. All 100 1st year MBBS students of regular batch of the year 2015 were enrolled, and given information about the proposal and objectives of the study. The data were collected on a semi-structured questionnaire distributed among these 1st year MBBS students. The questionnaire was in English only and consisted of questions associated to understanding of hepatitis-B infection as regard to basic information, epidemiological aspects and prevention of hepatitis-B related issues. All the questions were objective type with "Yes" or "No" as the options, although a less questions were of multiple-choice type. Knowledge was estimate through 12 questions. A scoring mechanism was used to understand overall knowledge level. Every correct answer was given one score and the range of the score varied between 0 (with no correct answer) and 12 (for all correct answers). Respondents with all correct answer got a maximum of 12 points, higher points indicate good knowledge. Based on total score, knowledge level was categorized into poor (≤5 points), average (6-8 points), and good (≥ 9 points). Apart from knowledge on hepatitis-B demographic profile such as age, sex, and marital status of the respondents were also recorded. Data entered into Microsoft Excel and analyzed using SPSS version - 18.0. The $P \leq 0.05$ was used for statistical significance. The response rates differed by item; hence the frequency issue was calculated using the similarity for the individual item.

RESULTS

Out of total 100 participants, 62% males and 38% were female.More than three-fourth (78%) were in the age group of 17-22 years followed by 40% in 17-19 years and (38%) in 20-22 years age, Two-third (64%) among all students were fully immunized for hepatitis-B (Table 1).

The majority (81.6%) of students had shown good level of knowledge, whereas 18.4% had average level of knowledge. 92% of students had correct knowledge regarding mode of transmission. However, 84% MBBS students could know about hepatitis. Half (52%) students could not gave the correct answer regarding scheduled of the vaccination. 88% respondents had correct knowledge about hepatitis-B transmitted from one person to another person. Although hepatitis-B vaccination was included in National Vaccination Program in India, but it was unexpectedly 52% students did not know the correct WHO schedule for hepatitis-B immunization (Table 2).

DISCUSSION

Hepatitis-B is an acute infection of liver caused by HBV. The lifespan chance of problems such as chronic hepatitis, cirrhosis, and hepatocellular carcinoma with chronic HBV infection is a vital concern for health-care personnel.[10,11] HBV infection is an occupational risk for physicians and surgeons mainly in developing countries where a carrier state is about 4% and kills about 1.1 million people globally every year. This study revealed that 81.6% MBBS students had shown good level of knowledge, whereas 18.4% had average level of knowledge. This may be attributed to coverage of topic in MBBS undergraduate curriculum. Similar finding by Khan *et al.*[12] and Darwish, and Al Khaldi[13] reported that the overall knowledge level

Table 1: Demographic characteristics and vaccination status of the study population

Particulars	*N* (%)
Age (in years)	
17-19	40 (40)
20-22	38 (38)
23-24	20 (20)
≥24	02 (02)
Gender	
Male	62 (62)
Female	38 (38)
Vaccination status	
Yes	64 (64)
No	36 (36)

Table 2: Gender wise distribution of respondent's knowledge about HBV infection of study sample (*N*=100)

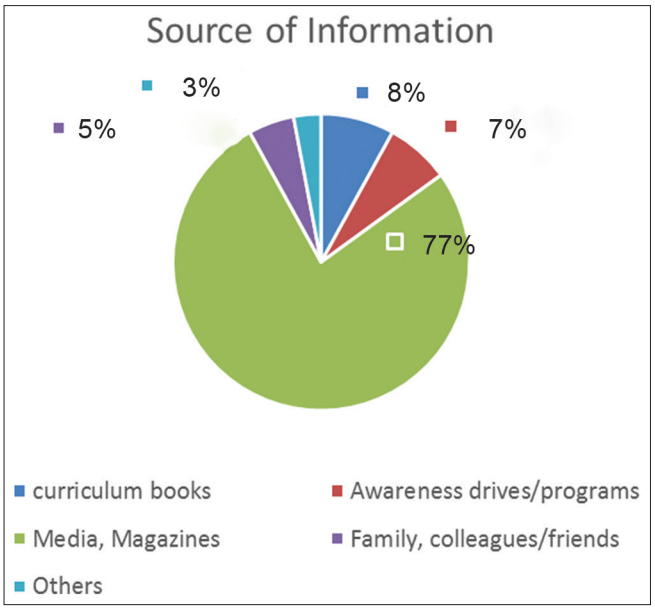
Question regarding knowledge	Correct answer			Incorrect answer			χ^2-value *P* value‡
	Male	Female	Total	Male	Female	Total	
Have you heard about hepatitis? (Yes)*	54	30	84	10	06	16	χ^2=0.000 *P*=1.000
What organs is primarily affected in hepatitis-B?*	58	32	90	07	03	10	χ^2=0.000 *P*=1.000
Can hepatitis-B transmitted from one person to another? (Yes)*	54	34	88	09	03	12	χ^2=0.359 *P*=0.549
If Yes, then what in your view is/are the mode (s) of its transmission? (Sexual and Parental)*	59	33	92	06	02	08	χ^2=0.053 *P*=0.816
What in your view can be possible outcomes of this disease?*	50	28	78	12	10	22	χ^2=0.321 *P*=0.570
Who are at higher risk of acquiring hepatitis?*	52	24	76	13	11	24	χ^2=1.062 *P*=0.302
Is hepatitis-B infection preventable by vaccination (Yes)*	56	34	90	04	06	10	χ^2=1.041 *P*=0.307
Do you know about PEP about hepatitis B? (Hepatitis-B vaccine and hepatitis-B immunoglobulin)*	46	28	74	16	10	26	χ^2=0.000 *P*=1.000
What is the schedule followed?*	25	23	48	36	16	52	χ^2=2.406 *P*=0.120
What was the source of information about this vaccine?*	55	22	77	12	11	23	χ^2=2.162 *P*=0.141
Did you ever come across anyone suffering from hepatitis among young relatives/friends/colleagues? (Yes)*	47	20	67	16	17	33	χ^2=3.570 *P*=0.058
Do you think you have sufficient knowledge regarding hepatitis? (Yes)*	28	16	44	40	16	56	χ^2=0.376 *P*=0.539

Data indicates both number and percentage, *Correct answer, ‡Value are significant *P*<0.05. HBV: Hepatitis-B virus

regarding hepatitis-B among medical students ranged between "good" and "average."

The majority (92%) of students had correct knowledge regarding mode of transmission of hepatitis-B in this study. Similar findings by Darwish and Al Khaldi[13] and Singh and Jain[14] among medical students declared that 77.7% and 86.7% of students had correct knowledge regarding mode of transmission of hepatitis-B, respectively. Another study done by Kasetty *et al.*[15] among dental professionals showed that 82.1% had correct knowledge regarding the mode of transmission. Whereas, a study done by Khan *et al.*[12] among medical students of Karachi, found that only 57.1% had correct knowledge regarding the same. It was declared that majority of respondents (84%) had heard of HBV infection, while only (16%) indicated they had not heard about the disease. The major source of information about HBV infection was the Media as indicated by most of the respondents (77%). Similarly, Hwang *et al* (2010)[16] found that about 87% of respondents had heard about HBV before and had extremely greater knowledge compared to those who had not heard about the disease.

In this study, 74% MBBS students had the correct knowledge regarding postexposure prophylaxis (PEP) for hepatitis-B. Similarly, a study by Kasetty *et al.*[15] found that 93.9% dental professionals had correct knowledge regarding PEP. However, in contrast, a study done by Khan *et al.*[12] revealed that 76% medical students did not have the knowledge regarding PEP. Low level of knowledge about postexposure treatment for hepatitis-B among the medical students was also found by Darwish and Al Khaldi.[13] Whereas, a study done by Singh and Jain[14] found that the majority of 3rd year undergraduate medical students gave correct answers, while only 20% of the 2nd year had the correct knowledge regarding the same. The most effective means to prevent HBV infection is through vaccination. Viral hepatitis is curable with effective vaccines, which is available since 1982 and has proven safe to both adults and children. In this study, two-third (64%) of MBBS students were fully immunized for hepatitis-B. However, 36% of students not immunized are the matter of concern. Similar results were observed in other studies also.[3,12] However, in contrast, a study conducted by Darwish and Al Khaldi[13] revealed that only 28.1% of medical students were vaccinated against HBV. The overall knowledge among MBBS students were satisfactory as compared to other studies but there was a gap which needs to be corrected regarding inclusion of hepatitis-B vaccination in national immunization program and even the correct WHO schedule for immunization, prevention and postexposure management of hepatitis-B.



CONCLUSION

HBV is a common but serious infectious disease of the liver. Hepatitis-B infection is an extensive health problem in the community. Theoretically, this study has provided some empirical evidence on knowledge and perception on HBV infection among 1st year MBBS students studying in IGIMS, Patna. The finding showed students were aware of HBV infection. It was also revealed that 81.6% MBBS students had shown good level of knowledge regarding hepatitis-B, and 64% of MBBS students are fully immunized for the same, which is matter of concern. Appropriate knowledge should be provided to the medical and other health-care professional students regarding HBV in the curriculum. Most important approach for prevention of occupational HBV infection is the use of hepatitis-B vaccine. Based on the results of this study, health authorities may plan awareness programs and interventions to improve the level of knowledge in MBBS students and health-care professionals and those with low level of knowledge about HBV vaccination to prevent the burden of this disease among this high-risk group.

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Original Article

Prevalence of Hepatitis B Virus Infection among Voluntary Blood Donors at a Tertiary Care Hospital Blood Bank - Tiruchirappalli

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Abstract

Background: Blood and blood products are an inseparable part of treatment in many medical settings. The most important infectious agents that are transmitted via blood transfusion are hepatitis B virus (HBV), hepatitis C virus, HIV, syphilis, and malaria for which there are screening tests performed as a routine in hospitals. The aim of this study was to determine the trend of seroprevalence of hepatitis B infection in voluntary blood donors in our institution.

Materials and Methods: This study was conducted at the blood bank of a tertiary care hospital serving the urban and rural population in and around Tiruchirappalli. A retrospective study on blood donors over a period of 3-year (January 2013-December 2015) was conducted to assess the seroprevalence and the trend of hepatitis B infection in voluntary blood donors in our institution. The second generation enzyme-linked immunosorbent assay was used to detect the antibodies to hepatitis B surface antigen in the donors as a marker of infection.

Results: A total of 27,343 voluntary donors over a period of 3-year were studied. 161 cases were positive with a prevalence of 0.58% which comes under "low prevalence (<2%) zone" as per WHO guidelines. Male donors showed higher seropositivity compared to female donors. Age wise seroprevalence was found to be more in 18-30 years age group.

Conclusion: Tamil Nadu has a low prevalence of hepatitis B in blood donors. Our study showed a decreasing trend in seroprevalence of hepatitis B. This could be due to effective preventive measures as well as improved health-care delivery systems. Our study revealed a high seroprevalence between the age group of 18 and 30 years. Better education of donors and improved prophylactic measures at public level must be done to ensure safe blood donation.

Key words: Blood donors, Hepatitis B, Infection

INTRODUCTION

Transfusion of blood and blood products as a specialized modality of patient management has been saving many lives. It is well known that there are complications that can occur due to blood transfusion. Some are only trivial and others are life-threatening, demanding for meticulous pre transfusion screening, and testing. The infection that could be transmitted by transfusion of unscreened blood includes hepatitis B virus (HBV), hepatitis C virus, HIV, syphilis, and malaria, etc. Knowledge of the various infectious agents with special emphasis on the disease endemic in that particular region is essential in understanding the strategies to prevent the transmission of this infection.

Hepatitis B is a major public health problem worldwide. These endogenous microbial agents transmitted by blood transfusion have the following characteristics:

- Long incubation period
- Carrier or latent state
- Ability to cause asymptomatic/sub clinical infection
- Viability and stability in stored blood or plasma
- The hall mark is the persistence of infection.

Approximately, 30% of world's population or about 2 billion persons have serological evidence of either current

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or last infection with HBV.[1] Countries are classified based on endemicity of HBV infection into high (8% or more), intermediate (2-7%) or low (<2%).[2] Assessment of the quality of donor selection and safety of the blood supply can be estimated by monitoring the prevalence of the serologic markers of infectious disease in screening tests. The prevalence of chronic HBV infection in India ranges from 2% to 10% is shown by different studies.[1,2] India, therefore, comes under the intermediate to high endemicity category. This infection is transmitted mainly through blood and blood products; vertically from mother to neonates and body secretions.[3] Factors such as viral load, in the blood components and immune status of the patient, and may play a role in viral transmission.[4]

Blood transfusion associated hepatitis B viral infection continues to be a major problem in India even after the adoption of mandatory screening of hepatitis B surface antigen (HBsAg) by enzyme-linked immunesorbent assay (ELISA).[3] Hepatitis B is caused by a DNA virus which infects the liver. The liver functions are impaired while the virus replicates in the hepatocytes. Hepatitis and liver damage arise as a consequence of immune response to virus in liver cells.[5] Some blood donors who were negative for surface antigen but positive for the core antibody have been reported to transmit HBV leading to acute hepatitis.[6] Despite all efforts including the use of a highly sensitive HBsAg test, transmission may still occur from apparently healthy blood donors. This may be attributed to the inability of the screening tests to detect HBsAg during a window period or as a result of the occult HBV infections (OBIs). OBI arises when the HBV DNA is detected, while HBsAg remaining undetectable. In about 20% of cases, the only positive marker is HBV DNA, but in other situations anti-HBs could be detected as well. Several factors may be involved in OBI, including mutated HBsAg, and low-level expression of HBsAg or entrapment of antigen in the circulatory immune complexes.[7,8]

HBV is present in blood, blood products and body fluid such as vaginal secretions and in low concentration in saliva of active carriers.[5] The average incubation period of the virus is 90 days from the time of exposure to onset of symptoms but may vary from 6 weeks to 6 months. This study aims to determine, the trends in hepatitis B infection in voluntary blood donors and compare it's prevalence among blood donors from other parts of India.[9,10]

Aims and Objectives

1. To study the seroprevalence of HBV infection among voluntary blood donors at blood bank MGM Government Hospital attached to KAPV Government Medical College, Tiruchirappalli, Tamil Nadu, India
2. Comparison with similar other studies.

MATERIALS AND METHODS

This study was conducted over a period of 3-year (January 2013-December 2015) at MGM hospital blood bank attached to KAPV Government Medical College, Tiruchirappalli. The study was conducted on voluntary blood donors who came to our blood bank and voluntary blood donation camps in and around Tiruchirapalli. All the blood donors, donating blood in the blood bank were considered as the study population. The family members, friends or relatives of the patients were categorized as replacement donors. People who donate blood without expecting any favor in return or in voluntary blood donation camps were classified as voluntary blood donors. Donors were screened by the standard criteria for donor fitness. They were carefully selected for donation by trained personnel after medical examination and a detailed pre-donation questionnaire form which included the donor register form, information regarding risk factor such as history of surgery, previous illness, hospitalization, and blood transfusion.

Inclusion Criteria

Clinically healthy individuals between 18 and 65 years of age with a body weight of above 45 kg and hemoglobin more than 12.5 g/dl with no significant medical or surgical history were qualified for the donation process.

Exclusion Criteria

Persons belonging to high-risk groups such as patients with chronic diseases, professional blood donors, drug abusers, dialysis patients, pregnant women, patients treated in thalassemia clinics, sexually transmitted disease clinics, and sex workers were excluded from the donation process.

After the blood collection, donor samples were obtained for serological testing. HBsAg screening was done using rapid test kit based on the principle of one step immunoassay. All reactive samples were tested again using the second generation the commercially available Erba Lisa ELISA kit with reported sensitivity of 100% and specificity of 99.9% per the manufacturer's manual. Samples showing repeat test reactivity on both methods were considered positive and were included for calculation of seroprevalence.

RESULTS

A total of 27,343 voluntary blood donors were recorded during our study period (January 2013-December 2015), out of which 25258 were males (92.37%) and 2085 were females (7.6%) (Table 1).

Of the 27,343 cases, 161 cases were found to positive for HBsAg. The prevalence was found to be 0.58%

constituting our area under lower risk group according to WHO guidelines.

Of the 161 cases were found to positive for HBsAg 155 cases were male donors and 6 were female donors, which accounts for prevalence of 0.61% in male donors and 0.29% female donors. Males outnumbered females in HBsAg positivity this could be due to less voluntary blood donation from the females (Table 2).

Our study showed that most of the HBsAg positive cases were in the age group of 18-30 years (74.5%) and the least in more than 50 years (1.2%) (Table 3).

Our study showed an increasing trend of hepatitis B positivity of 24.22% between 2013 and 2014, and a decrease of 6.2% between 2014 and 2015. However, this was not found to be significant as the $P < 1\%$ (Table 4).

DISCUSSION

Provision of safe blood is of paramount importance and its responsibility is solely with the blood transfusion service. Hepatitis B is a major health problem world wise and is associated with life-threatening complications. According to India's Drugs and cosmetics Act (1943), each blood unit has to be tested for hepatitis B infection.[2]

In our study among 27,343 blood donors screened the overall seroprevalence of HBsAg was observed to be 0.58% (total 161 cases) which is similar to study conducted by Remya *et al.*[11] and Gupta *et al.* (2004).[12-14]

According to the WHO classification Tamil Nadu qualifies as a low prevalence area (<2%) in voluntary blood donors. In comparison with studies conducted in other parts of India the prevalence rate is low[2] also in comparison with study conducted in Madurai our study showed a lower prevalence rate.[2]

Transfusion transmitted infection (TTI) Prevalence in India

Place	HBsAg %	Reference
Ludhiana	0.66	Gupta *et al*. (2004)[4]
Delhi	2.23	Pahuja *et al.* (2007)[8]
Lucknow (Uttar Pradesh)	1.96	Chandre *et al.* (2009)[13]
Southern Haryana	1.7	Arora *et al*. (2010)[11]
West Bengal	1.46	Bhattacharya *et al.* (2007)[11]
Bengaluru, Karnataka	1.86	Srikrishna *et al*. (1999)[14]
Present study	0.58	(2016)

In our study, the seroprevalence of HBsAg was significantly high in male donors (0.61%) as compared to female donors (0.29%), which is similar to that found in a study by Chandrasekhar *et al.* in 2000 at Madurai[15] and Remya *et al.*[11]

Table 1: Total donors

Year	Male	Female	Total
2013	6560	588	7148
2014	8723	698	9421
2015	9975	799	10,774
Total	25258	2085	27,343

Table 2: Donors positive for HBsAg

Year	Male	Female	Total
2013	31	-	31
2014	65	5	70
2015	59	1	60
Total	155	6	161

HBsAg: Hepatitis B surface antigen

Table 3: Age wise incidence of prevalence of HbSAg

Year	18-30	31-40	41-50	<51	Total
2013	25	06	-	-	31
2014	54	12	4	-	70
2015	41	13	4	2	60
Total	120	31	8	2	161

Table 4: Proportion of hepatitis B positive cases - year wise statistics

Year	Positive	Negative
2013	31	7117
2014	70	9351
2015	60	10,714
Total	161	27,182

In our study majority of sero positive donors were younger than 40 years, and the higher seroprevalence rate was observed in the age group of 18-30 years which is comparable with study conducted by Baba *et al.* in 2000[16] Taseema *et al.* in 2008[17] and Quadri *et al.* in 2013,[18] and Remya *et al.*[11]

On comparison of the trends of hepatitis B positivity among blood donors in 2013, 2014, and 2015 an increase in positive cases of 24.22% was noted between 2013 and 2014 while in the period of 2014 and 2015 a decrease of 6.2% was seen. However, this change was not found to be signification as value of $P < 1\%$. Rural population with lower literacy rate and a lack of awareness about the disease and its mode of prevention may be the reason for increased incidence. However, screening of blood bank donors for HBsAg does not totally eliminate the risk of HBV infection through blood transfusion. Since, the absence of this marker in the serum does not exclude the presence of HBV infection, who lacked detectable HBsAg but whose exposure to HBV infection was indicated by a

positive anti-HBc and HBV DNA, are a potential sources of HBV infection.[4]

Higher seroprevalence in youth in our study needs further re-intensification of preventive programs aimed at high-risk behavioral change, as this is the most productive and economically viable group of the population. Ensuring the safety of patients by reducing the residual risk of transfusion-transmitted hepatitis is the concern of every transfusion center. The introduction of 3rd generation sensitive test has reduced the incidence of post transfusion hepatitis B. However, the risk has not been eliminated. The risk of infection is higher in pooled plasma products. The risk of transmission of HBV can further be reduced by screening the blood donations for anti-HBC, as it is the only marker of HBV during the window period. Active HBV vaccination is another approach to reduce the rate of transmission of HBV. Public awareness, educational, and motivational programs, mass immunization programs ensuring 100% voluntary blood donation, implementation of strict pre-donation counseling, and donor selection criteria will be effective in decreasing the hepatitis B infection rate.

CONCLUSION

The low seroprevalence rate in our study, further recommends comprehensive screening of blood donors. With the advent of nucleic acid amplification techniques, western countries have decreased the risk of TTI to a major extent. However, the cost effectiveness is poor. NAT has added benefits but its high financial cost of concern. Since, our study revealed a high seroprevalence between the age group of 18-30, better education of donors and improved prophylactic measures at public level must be done to ensure safe blood donation. Immunization being the most effective and economic means of prevention along with education of high-risk group and health-care personnel reduce the risk of transmission. Proper pre-donation counseling and donor self-exclusion and 100% voluntary blood donation are some of the effective control measures.

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Original Article

Comparative Study of Epidural 0.75% Ropivacaine and 0.5% Levobupivacaine in Lower Limb Surgeries with Respect to Block Characteristics

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Abstract

Introduction: Epidural block during orthopedic surgery pain relief enables early post-operative mobilization, accelerates rehabilitation, and return to normal function.

Methods: After obtaining Ethical Committee approval and informed written consent from patients, the study was conducted on 70 patients of either sex, between 18 and 65 years of age and belonging to the American Society of Anesthesiologists Grade I and II physical status. Patient was divided into two groups Group R (ropivacaine) Group L and 20 ml of study drug given in each group.

Results: There was no significant difference in the sensory and motor block onset time between group R and L. The variations in the time duration of motor block between R (P = 0.028) and L (P = 0.043) was significant. The difference in the time of regression among the groups R and L was highly significant in both motor and sensory block parameters (P < 0.001). There was no marked difference in the duration of analgesia between the patients of group L and R.

Conclusion: Onset of sensory and motor block for levobupivacaine is delayed as compared with ropivacanie, whereas ropivacaine has shorter duration of motor block when compared with levobupivacaine

Key words: Block characterstics, Epidural, Levobupivacaine, Lower limb surgery, Ropivacaine

INTRODUCTION

Providing comfort to the patient by prevention and relief of pain and monitoring and maintenance of normal physiology during the perioperative period is the primary goal of an anesthesiologist.[1]

Epidural blockade is becoming one of the most useful and versatile procedures in modern anesthesiology. It is unique in that it can be placed at virtually any level of the spine, allowing more flexibility in its application to clinical practice. It is more versatile than spinal anesthesia, giving the clinician the opportunity to provide anesthesia and analgesia, as well as enabling chronic pain management. It provides better postoperative pain control and more rapid recovery from surgery.

For orthopedic surgery, the provision of pain relief enables early post-operative mobilization, accelerates rehabilitation, and return to normal function.[2]

Levobupivacaine and ropivacaine, the two new long-acting local anesthetics, have been developed as an alternative to bupivacaine, after the evidence of its severe toxicity. Both of these agents are pure left-isomers and, due to their three-dimensional structure, seem to have less toxic effects on the central nervous system (CNS) and on the cardiovascular system.

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Ropivacaine is developed as a pure S(-) enantiomer of ropivacaine. It is less lipophilic than bupivacaine and is less likely to penetrate large myelinated motor fibers resulting in a relatively reduced motor blockade. The reduced lipophilicity is also associated with decreased potential for CNS and cardiotoxicity. Thus, ropivacaine appears to be an important option for regional anesthesia and for the management of post-operative and labor pain.[3]

Levobupivacaine, the isolated S(-) enantiomer of bupivacaine, has been shown to be less cardiotoxic than bupivacaine in preclinical studies. Owing to the lower affinity of the S(-) isomer to the cardiac sodium channels compared to the R(+) isomer, it is associated with less cardiac side effects.[4]

Hence, in this study, we compared levobupivacaine 0.5% and ropivacaine 0.75% in epidural anesthesia in elective lower limb surgeries.

MATERIALS AND METHODS

After obtaining Ethical Committee approval and informed written consent from patients, the study was conducted on 70 patients of either sex, between 18 and 65 years of age and belonging to the American Society of Anesthesiologists (ASA) Grade I and II physical status.

Patients with the history of uncontrolled labile hypertension, heart block, dysrhythmia, on cardiac medication (adrenergic receptor antagonist, calcium channel blocker, or angiotensin-converting enzyme inhibitor), addiction to narcotic, patient posted for lower segment cesarean section and with any contraindication to epidural anesthesia were not included in the study.

1. Group R -20 ml of 0.75% ropivacaine
2. Group L - 20 ml of 0.5% levobupivacaine.

In each group, equal volume was injected. All patients were preloaded with 15 ml/kg of Ringer Lactate. In the operation theater pulse oximetry (Spo2), noninvasive blood/pressure and electrocardiogram were monitored and in sitting posture epidural catheter was placed into L2-L3 or L3-L4 epidural space under strict aseptic conditions, using Tuohy's needle with loss of resistance technique.

Onset, duration and quality of anesthesia were assessed. Sensory block was assessed bilaterally by short hypodermic needle in mid clavicular line motor block was assessed by modified bromage scale. The changes in above parameters were clinically and statistically compared.

Statistical Analysis

Results were expressed by standard methods, i.e., as mean ± standard deviation. Unpaired *t*-test was used for analysis in numerical data while for frequency Fisher exact test was applied. Statistical analysis was performed by SPSS (version 20.0). *P*-value was considered significant if <0.05 and highly significant if <0.001.

Study Design

Cross-sectional.

Study Period

November 2014 - May 2016.

Study Area

Patients posted for lower limb orthopedic surgeries.

Sample Size

70 patients, 35 in each group.

RESULTS

The objective of this study was to compare levobupivacaine 0.5% and ropivacaine 0.75% in epidural anesthesia in lower limb surgeries, with respect to onset and duration of motor blockade and sensory blockade, maximum dermatomal level of analgesia and time taken to achieve that.

As shown in Table 1 and Figure 1 group wise distribution of demographic data, like age, height, weight, body mass index (BMI), and sex were tabulated. On perusal of the same, we observe no significant deviation in any of these data among different groups of the cases. *P* value range was 0.067-0.982.

As shown in Table 2 and Figure 2, the mean sensory block onset time for the groups R and L was 9.9 ± 1.78 and 11.31 ± 1.5 min, respectively. The corresponding time figures for the motor block were 30.14 ± 5.6 and 29.8±5.3 min, respectively. There was no significant difference in the sensory block time between group R and L. The variation in the motor block time between two groups R and L were not significant.

Table 1: Group wise distribution of demographic data

Demographic data	Groups		
	Mean±SD		Significance (R*L)
	Group R	Group L	
Age* (year)	36.86±11.73	42.77±14.70	*P*=0.067
Height* (cm)	163.69±5.06	163.66±5.64	*P*=0.982
Weight* (kg)	64.31±6.23	64.46±5.36	*P*=0.918
BMI	23.82±1.49	24.04±1.27	*P*=0.505
Sex			
Male (%)	27 (77.14)	24 (68.57)	X^2=0.897, *P*=0.638
Female (%)	8 (22.86)	11 (31.43)	

SD: Standard deviation, *P<0.05

As shown in Table 3 and Figure 3, the duration of motor block for the patients of group R and L was 242 ± 71.6 and 278 ± 74 min, the time duration for sensory block was 388 ± 70.2 and 385 ± 72 min, respectively. The variations in the time duration of motor block between R and L was significant $P = 0.028$ and 0.043.

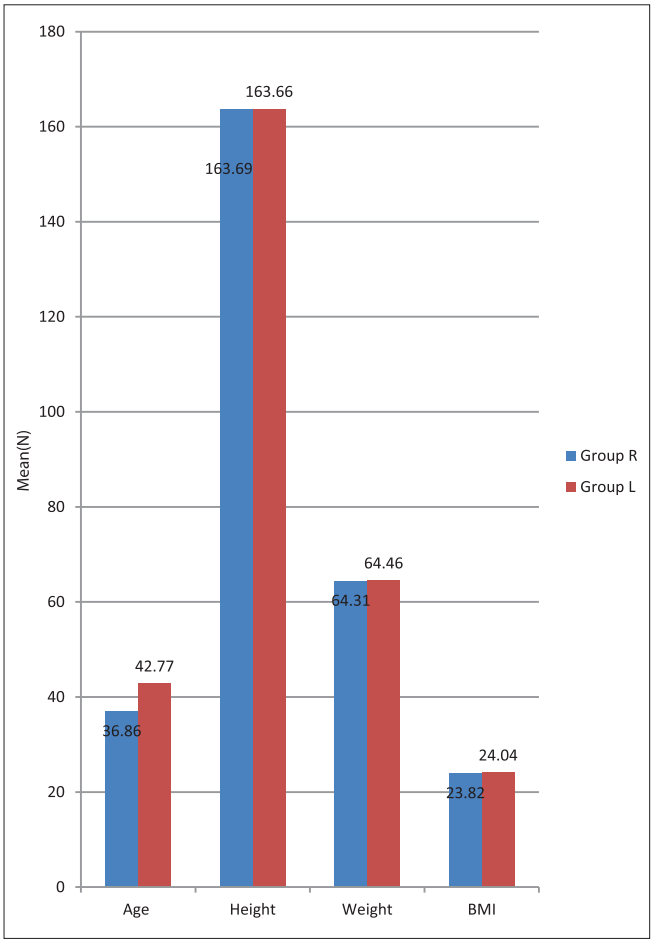

Figure 1: Demographic data groupwise

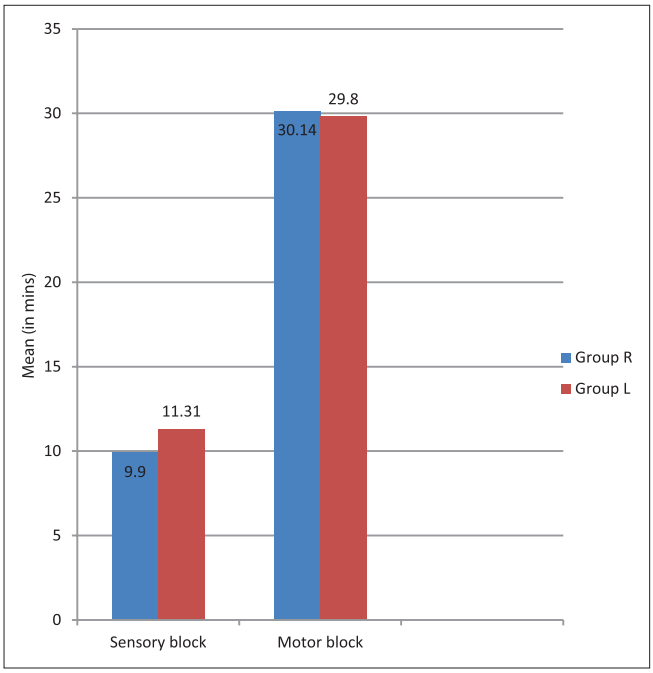

Figure 2: Time of onset of block

As shown in Table 4 and Figure 4, the time required for regression of sensory block in patients of the groups R and L was 84.6 ± 4.47 and 192.2 ± 17.01 min, respectively, the corresponding regression time required for motor blocks was 81.37 ± 5.52 and 124.57 ± 11.88 min. The difference in the time of regression among the groups R and L was highly significant in both the parameters $P < 0.001$.

As shown in Table 5 and Figure 5, sensory levels of T6 to T10 segments were recorded in the table. The highest sensory level of T7 segment was found in 18 (51.43%) and 10 (28.57%), respectively, members of each of the groups. The variation in the sensory level among the members of different groups, in respect of each of these segments, was however not significant $P = 0.53$.

As shown in Table 6, duration of analgesia was respectively 218 ± 19.3 and 213 ± 20 min for members of group R and L. There was no marked difference in the duration of analgesia between the patients of group L and R.

DISCUSSION

Levobupivacaine and ropivacaine, the two new long-acting local anesthetics, have been developed as an alternative to bupivacaine, after the evidence of its severe toxicity. Both of these agents are pure left-isomers and, due to their three-dimensional structure, seem to have less toxic effects on the CNS and on the cardiovascular system.

Table 2: Onset of sensory block and motor block among the groups

Onset time of block	Mean±SD (min)		Significance (R*L)
	Group R	Group L	
Sensory block	9.9±1.78	11.31±1.5	*P*=0.001 *T*=−3.4
Motor block	30.14±5.6	29.8±5.3	*P*=0.713 *T*=0.369

SD: Standard deviation

Table 3: Duration of motor block and duration of sensory block among the groups

Duration (in min)	Mean±SD (min)		Significance (R*L)
	Group R	Group L	
Duration of motor block	242±71.6	278±74	*P*=0.043
Duration of sensory block	388±70.2	385±72	*P*=0.853

SD: Standard deviation

Table 4: The time regression of blocks among the groups

Time of regression of block (min)	Groups		
	Mean±SD (min)		Significance (R*L)
	Group R	Group L	
Sensory block	84.6±4.47	192.2±17.01	*P*=0.001
Motor block	81.37±5.52	124.57±11.88	*P*≤0.001

SD: Standard deviation

Table 5: Highest sensory level among the groups

Highest sensory level (N)	Groups		
	Mean±SD (%)		Significance
	Group R	Group L	
T6	5 (14.29)	5 (14.29)	X^2=7 *P*=0.53
T7	18 (51.43)	10 (28.57)	
T8	8 (22.86)	8 (22.86)	
T9	2 (5.71)	5 (14.29)	
T10	2 (5.71)	7 (20.00)	

SD: Standard deviation

Table 6: Duration of analgesia among the groups

Duration of analgesia	Groups (R*L)		
	Mean±SD		Significance
	Group R	Group L	
Duration of analgesia (in min)	218±19.3	213±20	*P*=0.273

SD: Standard deviation

Demographic Details

Group R receiving 20 ml of 0.75% ropivacaine, group L receiving 20 ml of 0.5% levobupivacaine. Distribution of demographic data - such as age, height, weight, BMI, and sex - were observed, on perusal of the same we observe no significant deviation in any of these data among different groups of the cases. An Indian study by Kameshwara Rao *et al.*[5] reported that patients studied in the three groups did not vary much with respect to age, sex or weight.

Block Characteristics

In our study, the mean time for onset of sensory block in ropivacaine group was 9.9 ± 1.78 min and 11.31 ± 1.5 min in levobupivacaine group. The mean time for onset of motor block in ropivacaine group was 30.14 ± 5.6 min and 29.8 ± 5.3 min in levobupivacaine group. There was no significant difference in the sensory block onset time between the groups ($P > 0.05$). The variation in the motor block onset time between the two groups was not significant ($P > 0.05$). Casati *et al.*[6] conducted study on 45 ASA I-III patients undergoing elective hip replacement surgery comparing epidural block with 10 ml of 0.5% levobupivacaine, 0.5% bupivacaine, or 0.5% ropivacaine found no difference in the time of onset of sensory and

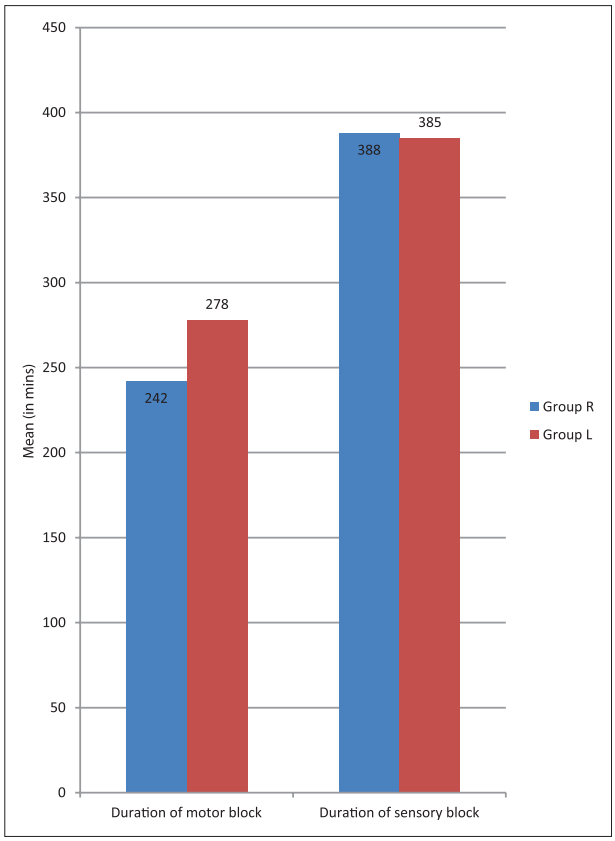

Figure 3: Time of duration of motor and sensory block

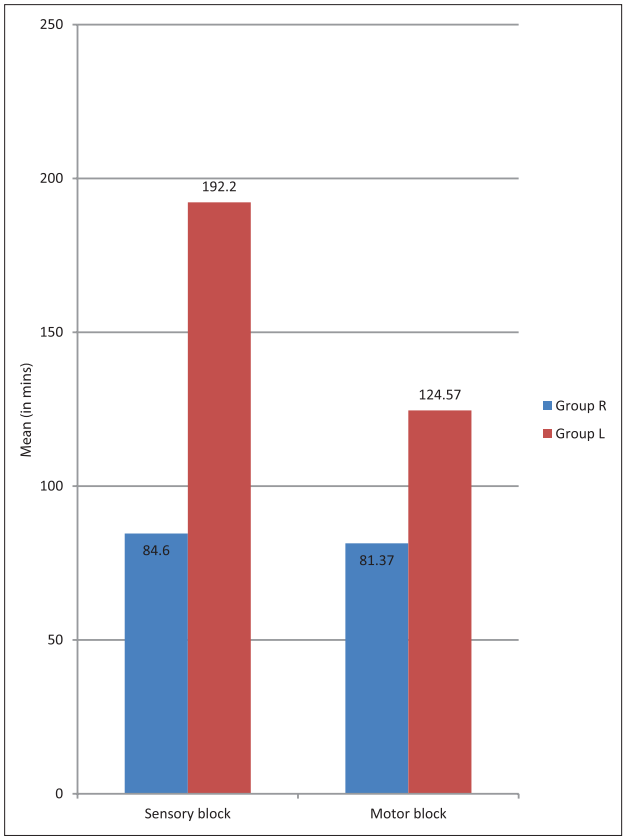

Figure 4: Time of regression of block

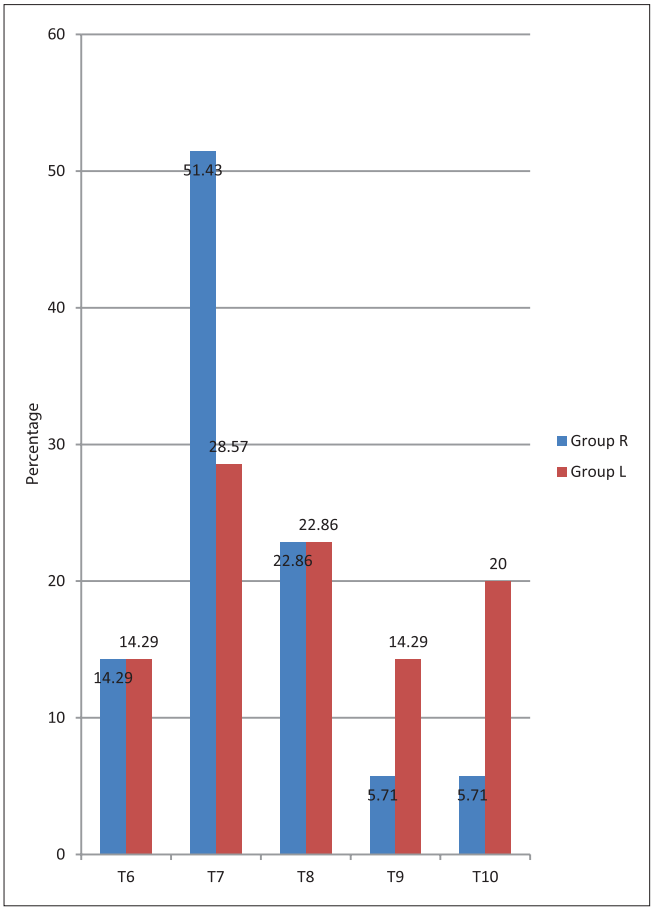

Figure 5: Highest sensory level

motor block. Peduto *et al.*[7] conducted study on 65 adult patients of ASA I-III undergoing elective lower limb procedures with 15 ml of 0.5% epidural Levobupivacaine or 15 ml of 0.75% epidural ropivacaine. They observed that the onset of sensory block was similar in both groups.

Duration of motor blockade was assessed from the time of administration of drug to complete motor recovery. In our study, the mean duration of motor block in ropivacaine group was 242 ± 71.6 min and in levobupivacaine group was 278 ± 74 min. The variations in the time duration of motor block between ropivacaine and levobupivacaine group were significant ($P < 0.05$). Brockway *et al.*[8] showed that motor block produced by ropivacaine was slower in onset. The mean duration of motor blockade of ropivacaine is lower than that of levobupivacaine.

It was concluded that levobupivacaine 0.5% produces a motor block deeper than that produced by 0.5% ropivacaine.[9] Our results are similar to a study done by David L Brown.[9] where the duration of motor block with 20 ml of 0.5% ropivacaine was 220 ± 52 min and 0.5% bupivacaine was 276 ± 52 min and thus of longer duration. Zaric *et al.*[10] found that motor blockade with 0.75% ropivacaine was comparable to 0.5% bupivacaine. Brown *et al.* and Cekmen *et al.*[11] showed that duration of motor block was significantly longer in the 0.5% bupivacaine group as compared to 0.5% ropivacaine. Zaric *et al.*[10] found that motor blockade with 0.75% ropivacaine was comparable to 0.5% bupivacaine. De Negri[12] *et al.* conducted prospective, randomized, observer-blinded clinical trial, and compared the incidence of unwanted lower extremity motor blockade and the analgesic. He concluded no difference in post-operative analgesia with the drugs.

The mean duration of sensory analgesia in ropivacaine group was 388 ± 70.2 min and in levobupivacaine group was 385 ± 72 min. Casati *et al.*[6] conducted study on 45 ASA I-III patients undergoing elective hip replacement surgery comparing epidural block with 10 ml of 0.5% levobupivacaine, 0.5% bupivacaine or 0.5% ropivacaine. It was found that there was no significant difference in the duration of sensory analgesia among all the groups. Peduto *et al.*[7] conducted study on 65 adult patients of ASA 1-3 undergoing elective lower limb procedures and were given epidural levobupivacaine 0.5% 15 ml or epidural ropivacaine 0.75% 15 ml. The duration of sensory blockade in both the groups was similar as reported by Peduto *et al.* Higher concentration of levobupivacaine (i.e., 0.75%) provides a longer duration of sensory and motor block without any increase in the incidence of adverse side effects.[6]

The highest sensory level of T7-T8 segment was found to be 74.3% and 51.4%, respectively, among the members of each of the groups (as named R, L) respectively. The variation in the sensory level among the members of different groups, in respect of each of these segments was however not significant. Chandran *et al.* also reported that the mean maximum sensory level reached was T8 in ropivacaine and bupivacaine groups with the volume administered.[13] An Indian study reported that there was no difference in highest level of sensory blockade in the three groups.[5] Few studies reported, equal doses of levobupivacaine and bupivacaine (15 ml of 0.5%) provide maximum cephalic spread (T7-T8) and duration of analgesia (4-6 h).[14]

CONCLUSION

It can be concluded that onset of sensory and motor block for levobupivacaine is delayed as compared with ropivacanie. Ropivacaine has shorter duration of motor block when compared with levobupivacaine. Thus, ropivacaine and levobupivacaine both can be used as an alternative to bupivacaine.

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Original Article

Comparison of Intensive Care Unit Sedation Using Dexmedetomidine, Propofol, and Midazolam

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Abstract

Introduction: This study compares the effectiveness of dexmedetomidine for the sedation of patients admitted to our intensive care unit (ICU) with propofol and midazolam in respect to tracheal extubation and length of stay in ICU and to study changes in heart rate (HR), mean arterial pressure, SpO_2 during and after sedation.

Materials and Methods: A total of 90 patients randomized into three groups of 30 to receive either dexmedetomidine, propofol, or midazolam drug. The dexmedetomidine group loading dose was 0.5-1 μg/kg per 10 min, followed by maintenance infusion at 0.1-1 μg/kg/h. The propofol group received a loading dose of 0.5-1 mg/kg followed by an infusion of 25-75 mcg/kg/min. The midazolam group received an infusion of 0.012-0.024 mg/kg/h. Respiratory rate, HR, blood pressure, Ramsay sedation score, tramadol need, saturation, time to extubation, duration in ICU were monitored and recorded all through the ICU stay.

Results: Hypotension occurred in 6.4% patients in dexmedetomidine group, 14.22% in propofol group, and 5% in midazolam group. Bradycardia occurred in 7.5% patients receiving dexmedetomidine at the time of loading of drug. During sedation mean pulse rate in dexmedetomidine group was 77.54 ± 9.34, in propofol group 89.34 ± 10.1 and for midazolam group 90.23 ± 10.7. Reduced time to tracheal extubation for dexmedetomidine group (7.4 ± 1.85) h, for propofol (5.6 ± 1.56) h compared to midazolam (16.9 ± 15.62) h.

Conclusion: Dexmedetomidine is a satisfactory agent for sedation in ICU. Dexmedetomidine provides hemodynamic stability and has no clinically important adverse effects on respiration. The mean time from cessation of sedation to tracheal extubation was shorter for dexmedetomidine and propofol treated patients than from midazolam treated patients.

Key words: Anaesthesia, Dexmedetomidine, Diastolic blood pressure, Heart rate, Midazolam, Propofol, Respiratory rate, SpO_2, Systolic blood pressure, Time to tracheal extubation

INTRODUCTION

Patients in an intensive care unit (ICU) are exposed to a variety of noxious stimuli including pain after surgery, frequent venipuncture, and discomfort from the presence of an endotracheal tube. Sedation is frequently required as a component of compassionate care in these patients. Promotion of rest and sleep in critically ill patients facilitates healing. Multisystem adverse effects of sleep deprivation have been reported. Physical activity also plays a pivotal role in recovery and long-term outcomes.

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Other goals of adequate sedation include optimizing safety for patients and caregivers, facilitating mechanical ventilation, reducing anxiety and delirium, inducing sleep, and, ultimately, providing comfort and safety.

The sedatives used most often include propofol and midazolam. These medications provide adequate sedation but also can cause oversedation. Oversedation can lead to prolonged duration of mechanical ventilation, longer ICU and hospital stays, increased incidence of ventilator-associated pneumonia, and inability of patients to communicate with health-care providers or family members.

Undersedation is also harmful and can lead to anxiety, ventilator dysynchrony, dislodged equipment, delirium, increased oxygen consumption, and hyperactivity. Making the distinction between too much sedation and not enough sedation can sometimes be difficult when propofol and midazolam is used.

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For decades, gamma-aminobutyric acid (GABA) receptor agonists (including propofol and benzodiazepines such as midazolam) have been the most commonly administered sedative drugs for ICU patients worldwide. Despite the well-known hazards associated with prolonged use of GABA agonists, few investigations of ICU sedation have compared these agents to other drug classes. Instead, the recent focus in the practice of critical care sedation has been on nurse-implemented algorithms and drug-interruption protocols to optimize drug delivery, regardless of class. These protocols and algorithms are promising but not uniformly beneficial, and their adoption into routine practice has been slow.

Inadequate sedative techniques may adversely affect morbidity and even mortality in the ICU, and the search for the ideal sedative agent continues. The ideal agent should satisfy the physician's desire for an effective, safe, titratable, cheap, and rapidly acting drug that has both sedative and analgesic properties and should also prevent anxieties and unpleasant memories for the patient. The published accounts of patients' recollections of the ICU are on the whole reassuring, but adverse experiences, such as physical discomfort from procedures, inability to communicate and lack of sleep, continue to feature prominently. Thus, when a new sedative agent is compared with the currently used sedative drugs in the ICU, its pharmacokinetic and pharmacodynamic properties will, of course, be contrasted. More importantly, both the physician's and the patient's perceptions of its efficacy require investigation.

The alpha-2 agonist dexmedetomidine is a new sedative and analgesic agent which has been licensed recently in the USA as ICU sedation for up to 24 h after surgery. Dexmedetomidine provides hemodynamic stability and appears to have no clinically important adverse effects on respiration. Its sedative properties are unique in that it produces only mild cognitive impairment, allowing easy communication between health-care provider and patient in the ICU. We therefore compared the sedative and analgesic properties, safety profile, cardiovascular responses, ventilation and extubation characteristics, and patient perceptions of dexmedetomidine with those of the commonly used agents propofol and midazolam in the ICU.

MATERIALS AND METHODS

Trial Design

After approval from Ethical Committee and written informed consent of the patient, 90 patients of both gender were recruited for the study. This study was randomized. Open label trial conducted in the ICU in Basaveshwar Teaching and General Hospital, Kalaburagi. ICU has 24 h coverage by resident house staff. Assessment as to whether patients would require sedation for short term (<24 h), medium term (>24-<72 h) or long term >72 h) mechanical ventilation on admission to ICU was done. Patients stratified by predicted sedation time while receiving mechanical ventilation were randomized and were entered into trial.

Eligibility Criteria

Inclusion criteria

- Patients of either gender
- Patients >18 years of age
- Patients who require immediate sedation as to permit the initiation and tolerance of mechanical ventilation.

Exclusion criteria

- Known or suspected allergy or intolerance to dexmedetomidine, propofol or midazolam
- Pregnancy
- Head injury
- Patient currently treated with or been treated with alpha-2 agonist and blockers
- Status epilepticus
- Coma due to cerebrovascular accidents or unknown etiology
- Acute unstable angina
- Acute myocardial infarction.

Material used

i. Injection dexmedetomidine
ii. Injection propofol
iii. Injection midazolam.

Method

Patient enrolled in the study divided into three groups. There are 30 patients allocated for each group.

Group 1: Patient randomized in dexmedetomidine group received a loading dose of dexmedetomidine 0.5-1 mcg/kg over 10 min followed by a maintenance infusion of 0.1 to 1 mcg/kg/h. The rate of the maintenance was subsequently titrated to achieve a target Ramsay sedation score that was specified for each for each patient response to therapy.

Group 2: Patients randomized to the propofol group received a loading dose of 0.5-1 mg/kg then an infusion of 25-75 mcg/kg/min was adjusted to achieve the target Ramsay sedation score. As for the propofol group in situations in which rapid control of sedation was required an infusion bolus could be administered.

Group 3: Patients randomized in midazolam group received an infusion of 0.012-0.024 mg/kg/h adjusted to achieve

the target Ramsay sedation score. Situations in which rapid control of sedation was required an infusion bolus could be administered.

Only tramadol 1 mg/kg was given to patients of all the three groups as analgesic agent.

Measurement Scales

The Ramsay sedation score was used to quantitate the desired degree of sedation, specified at the regular intervals and adjusted as the patient's condition (i.e., recovery or deterioration) dictated. Patients were maintained at Ramsay sedation score of >2 by adjustments to the sedative regimens. Patients receiving muscle relaxants and sedation were given a Ramsay sedation score of 6.

Measurements

The Ramsay sedation score (target and actual) was recorded hourly for the first 72 h or up to the time of discharge from ICU if this occurred before 72 h. After 72 h, it was recorded as the patient's condition or infusion rate was altered. Time to tracheal extubation, time to ICU discharge and requirements of reintubation were recorded. A record of vital signs was maintained every 20 min for 40 min, then every 6 h for 48 h following extubation or until ICU discharge, whichever comes first. Decisions as to when a patient was ready for a trial of extubation or for discharge from the ICU were left to the attending intensivists.

Ramsay described Ramsay sedation scale to judge sedation level in critically ill patients.

Ramsas Sedation Score

Awake

1. Anxious and/or agitated
2. Cooperative, oriented and tranquil
3. Response to command.

Asleep

1. Quiescent with brisk response to light glabellar tap or loud auditory stimulus
2. Sluggish response to light glabellar tap or loud auditory stimulus
3. No response.

Complications which occurred as a result of patient's conditions, mechanical ventilation or infusion of sedative agent were recorded in all the three groups.

Primary Outcome Measures

The time from withdrawal of sedation until tracheal extubation and ICU discharge for each stratum was taken as the primary outcome measures. The situations in which patients required multiple independent periods of sedation or reintubation due to alterations in their disease processes, the first period of sedation accompanied by tracheal extubation was utilized for data collection surrounding this event. Data were collected for the duration of the patient ICU stay. ICU length of stay was recorded as the time from admission to ICU until the patient was discharged.

Statistical Analysis

All statistical analyses were performed using INSTAT for windows. Continuous variables were tested for normal distribution by the Kolmogorov-Smirnov test. Data were expressed as either mean and standard deviation or numbers and percentages. All the data were compared with one-way analysis of variance (ANOVA).

RESULTS

These Table 1 and Figure 1 show distribution of patients according to age in all groups. The mean and standard deviation of age in all groups have been demonstrated. There was no statistically significant difference in age distribution in any group (P >0.05).

M:F ration for dexmedetomidine = 1.3:1

M:F ratio for proposal = 1.5:1

M:F ratio for midazolam = 1.4:1

Male = 51 female = 39 Total = 90 (Table 2 and Figure 2).

Table 1: Age distribution

Age (years)	*n* (%)		
	Dexmedetomidine	Propofol	Midazolam
18-30	8 (26)	12 (40)	9 (30)
31-45	12 (40)	9 (30)	10 (34)
46-60	10 (34)	9 (30)	11 (36)
Mean	37.03	36.7	37.9
Standard deviation	12.75	12.18	12.48

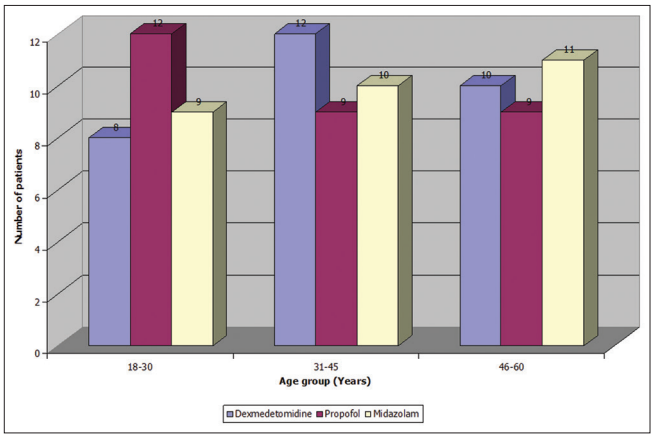

Figure 1: Age distribution

These Table 3 and Figure 3 show distribution of patients according to weight in all age groups.

- The mean and standard deviation of weight in all age groups have been demonstrated.
- There was no significant difference in weight distribution in any age group ($P > 0.05$).

P value is calculated by one-way ANOVA. Baseline pulse rate in all three groups is not statistically significant ($P > 0.05$).

During Sedation

P value during sedation is <0.001 means statistically significant difference is present among the groups.

From Stoppage of Sedation of Extubation

$P < 0.001$ means statistically significant difference is present among the groups.

At Extubation

$P < 0.001$ means statistically significant difference is present among the groups.

From Extubation to ICU Discharge

$P > 0.05$ means there is no significant difference present among the groups (Table 4 and Figure 4).

This Table 5 shows the mean changes in respiratory rate in all groups. The difference in respiratory rate was not significant at baseline, during sedation, from stoppage of sedation to extubation and extubation to ICU discharge. Difference among the groups calculated by ANOVA test is not statistically significant ($P > 0.05$).

These Table 6 and Figure 5 show the mean changes in systolic blood pressure (SBP) in Dexmedetomidine, propofol, and midazolam group.

Table 2: Sex distribution

Sex	*n* (%)		
	Dexmedetomidine	Propofol	Midazolam
Male	17 (56)	18 (60)	16 (54)
Female	13 (44)	12 (40)	14 (46)
Total	30	30	30

Table 3: Weight distribution

Weight (kg)	*n* (%)		
	Dexmedetomidine	Propofol	Midazolam
35-54	8 (26)	9 (30)	12 (40)
55-74	13 (44)	12 (40)	9 (30)
75-95	9 (30)	9 (30)	9 (30)
Mean	64.56	64.3	62.2
Standard deviation	13.02	15.7	14.11
Total	30	30	30

At all times, the difference is SBP among all the three groups calculated by ANOVA test is not statistically significant ($P > 0.05$).

These Table 7 and Figure 6 show mean changes in diastolic BP in dexmedetomidine, propofol, and midazolam group. At all times, the difference is SBP among all the three groups calculated by ANOVA test is not statistically significant ($P > 0.05$).

These Table 8 and Figure 7 show mean changes in mean BP in all the three groups. At all times difference in mean BP among all the three groups calculated by ANOVA test is not statistically significant ($P > 0.05$).

This Table 9 shows mean changes in SPO_2 dexmedetomidine, propofol, and midazolam group. At all times the difference in SPO_2, BP among all the three groups calculated by ANOVA test is not statistically significant ($P > 0.05$).

This Figure 8 shows the mean time (h) from cessation of sedation to extubation for dexmedetomidine is 7.4 h, for propofol is 5.6 h and for midazolam is 16.9 h.

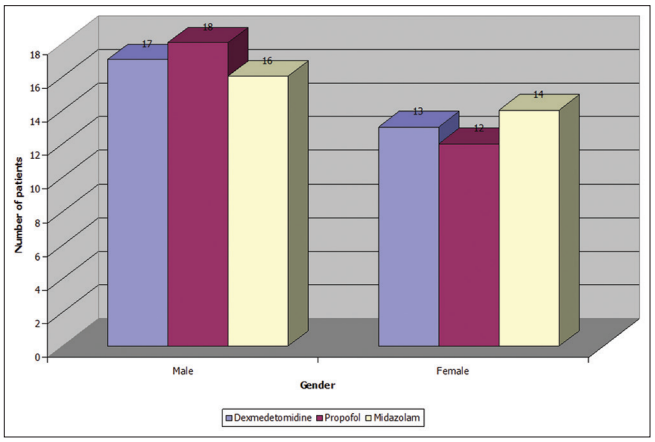

Figure 2: Sex distribution

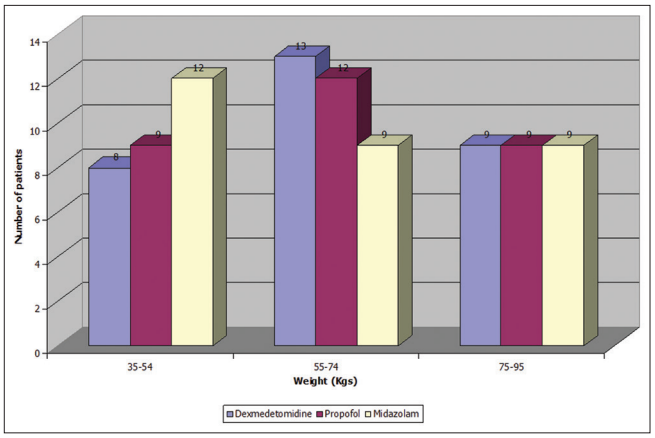

Figure 3: Weight distribution

Table 4: Mean changes in pulse rate

Sedative used/ SD of PR	Baseline	During sedation	From stoppage of sedation to extubation	At extubation	From extubation to ICU discharge
Dexmedetomidine	92.00	78.26	83	84.7	89.21
Standard deviation	3.7	4.97	2.56	2.27	0.75
Propofol	92.26	85.66	92.33	94.23	92.49
Standard deviation	3.55	3.02	1.74	1.47	0.84
Midazolam	92.6	84.93	93.86	94.4	92.45
Standard deviation	3.64	2.21	1.814	1.32	0.85
P value	>0.05	<0.0001	<0.0001	<0.0001	>0.05

ICU: Intensive care unit, SD: Standard deviation

Table 5: Mean changes in systolic blood pressure

Sedative used/ SD of SBP	Baseline	During sedation	From stoppage of sedation to extubation	At extubation	From extubation to ICU discharge
Dexmedetomidine	132.7	121.6	125.8	126.9	119.8
Standard deviation	11.1	8.61	8.88	9.47	9.5
Propofol	134.8	118.8	127.4	128.2	121.4
Standard deviation	11.5	10.1	10.09	10.10	9.26
Midazolam	134.3	123.6	126.9	128.4	122.9
Standard deviation	15.2	8.79	9.74	8.78	9.17
P value	>0.05	>0.05	>0.05	>0.05	>0.05

ICU: Intensive care unit, SD: Standard deviation

Table 6: Mean changes in respiratory rate

Sedative used/ SD of RR	Baseline	During sedation	From stoppage of sedation to extubation	At extubation	From extubation to ICU discharge
Dexmedetomidine	18.83	13.93	14.5	14.46	14.6
Standard deviation	1.36	0.78	0.5	0.5	0.56
Propofol	18.46	14	14.56	14.5	14.5
Standard deviation	2.36	0.83	0.5	0.5	0.50
Midazolam	18.56	13.93	14.53	14.56	14.53
Standard deviation	1.04	0.78	0.5	0.5	0.50
P value	>0.05	>0.05	>0.05	>0.05	>0.05

ICU: Intensive care unit, SD: Standard deviation

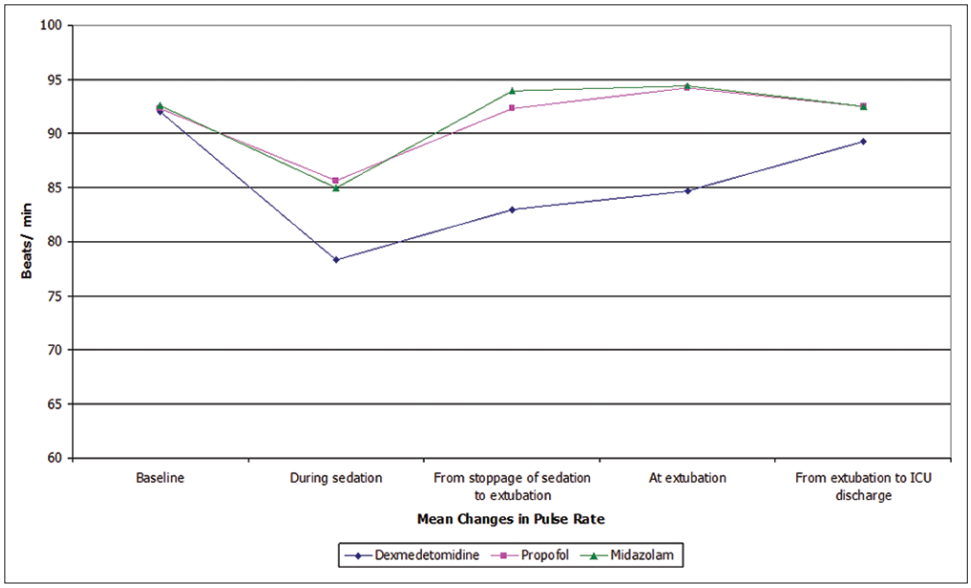

Figure 4: Mean changes in pulse rate

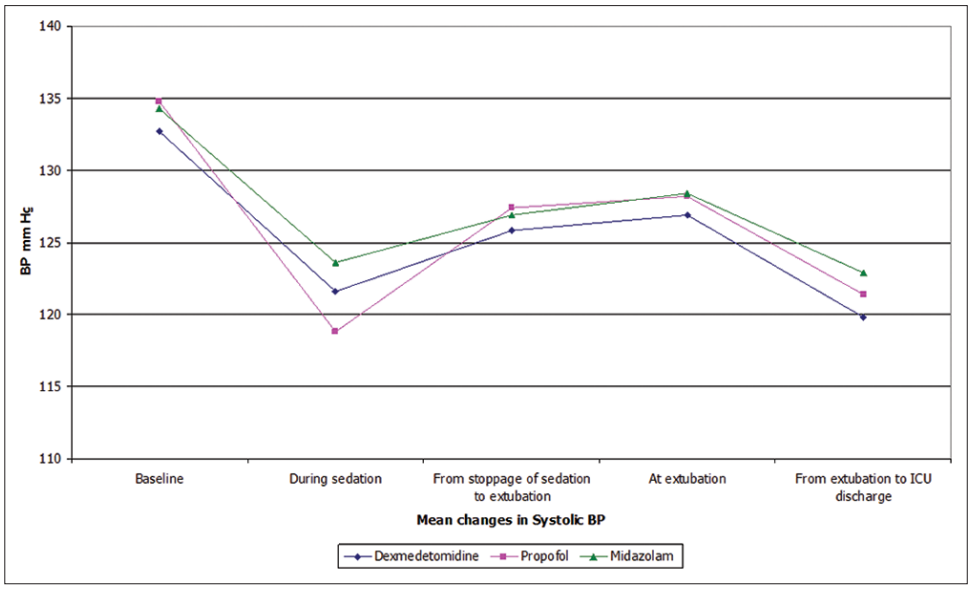

Figure 5: Mean changes in systolic blood pressure

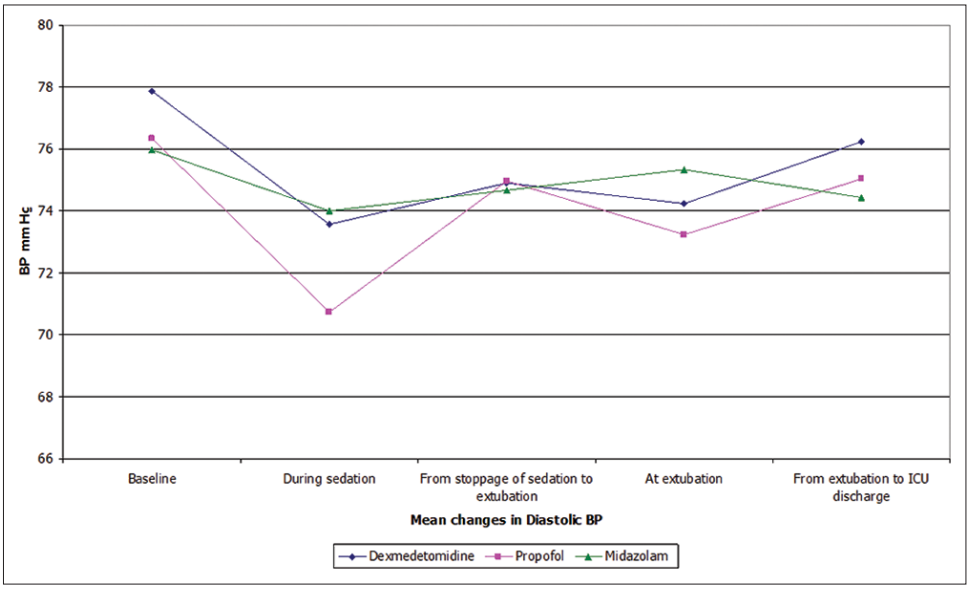

Figure 6: Mean changes in diastolic blood pressure

P value of dexmedetomidine, propofol, and midazolam group is <0.001, which is statistically significant.

This Figure 9 shows cessation of sedation to ICU discharge for dexmedetomidine its 83 h for propofol is 92 h and for midazolam it is 78 h.

P value calculated by ANOVA test among all the three groups is >0.05 which is statistically not significant.

DISCUSSION

This study was considered to assess the efficacy of a new drug dexmedetomidine with propofol and midazolam, established i.v., sedative agent regularly used in ICU in terms of changes in vitals, duration of extubation ICU discharge and complications.

The alpha-2 agonist dexmedetomidine is a new sedative and analgesic agent which has been licensed recently in the USA as ICU sedation for up to 24 h after surgery. Dexmedetomidine provides hemodynamic stability and appears to have no clinically important adverse effects on respiration. Its sedative properties are unique in that it produces only mild cognitive impairment, allowing easy communication between health-care provider and patient in the ICU. We therefore compared the sedative and analgesic properties, safety profile, cardiovascular

Table 7: Mean changes in diastolic blood pressure

Sedative used/ SD of DBP	Baseline	During sedation	From stoppage of sedation to extubation	At extubation	From extubation to ICU discharge
Dexmedetomidine	77.87	73.56	74.89	74.23	76.22
Standard deviation	8.40	7.40	7.26	6.96	6.01
Propofol	76.32	70.75	74.98	73.23	75.04
Standard deviation	7.56	7.56	6.47	7.14	6.90
Midazolam	75.98	73.99	74.67	75.33	74.44
Standard deviation	8.03	7.48	6.95	7.36	6.09
P value	>0.05	>0.05	>0.05	>0.05	>0.05

ICU: Intensive care unit, SD: Standard deviation

Table 8: Mean changes in mean blood pressure

Sedative used/ SD of MBP	Baseline	During sedation	From stoppage of sedation to extubation	At extubation	From extubation to ICU discharge
Dexmedetomidine	96.21	89.23	89.78	90.11	89.98
Standard deviation	5.98	6.11	6.07	7.46	4.69
Propofol	95.56	86.86	86.21	87.73	88.78
Standard deviation	6.85	5.48	4.38	5.27	5.69
Midazolam	95.11	90.99	90.54	90.11	89.99
Standard deviation	7.91	6.49	6.17	6.11	5.42
P value	>0.05	>0.05	>0.05	>0.05	>0.05

ICU: Intensive care unit, SD: Standard deviation

Table 9: Mean changes in SpO_2

Sedative used/ SD of SpO_2	Baseline	During sedation	From stoppage of sedation to extubation	At extubation	From extubation to ICU discharge
Dexmedetomidine	98.33	98.78	98.21	98.99	98.11
Standard deviation	0.95	0.68	0.71	0.64	0.63
Propofol	97.6	98.21	98.34	98.22	98.1
Standard deviation	1.08	0.58	0.66	0.63	0.63
Midazolam	96.99	97.1	98.34	98.21	98.85
Standard deviation	0.93	0.62	0.63	0.60	0.66
P value	>0.05	>0.05	>0.05	>0.05	>0.05

ICU: Intensive care unit, SD: Standard deviation

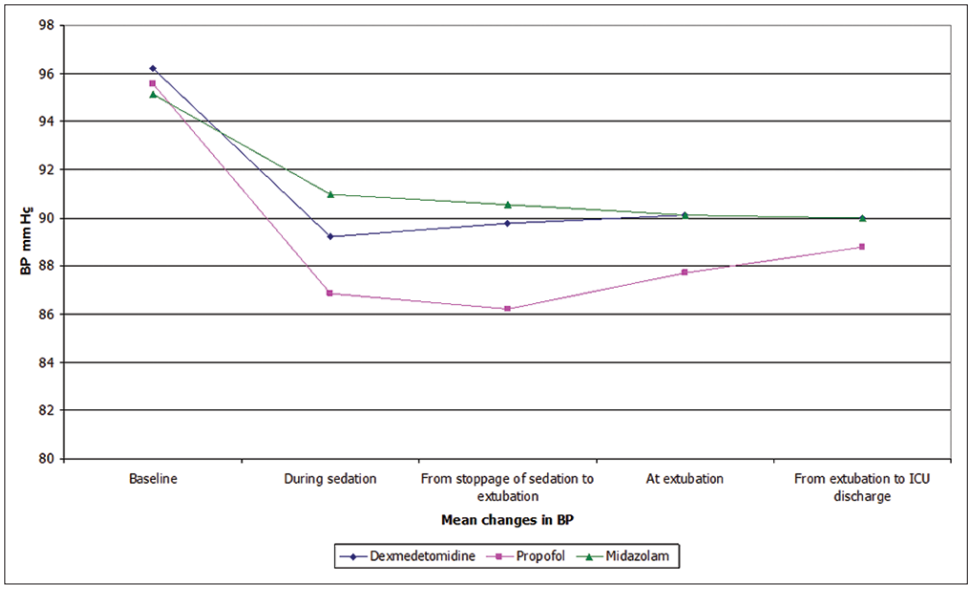

Figure 7: Mean changes in mean blood pressure

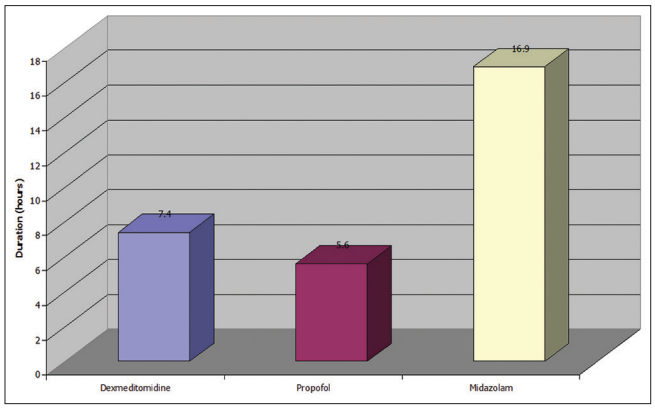

Figure 8: Duration from cessation of sedation to extubation

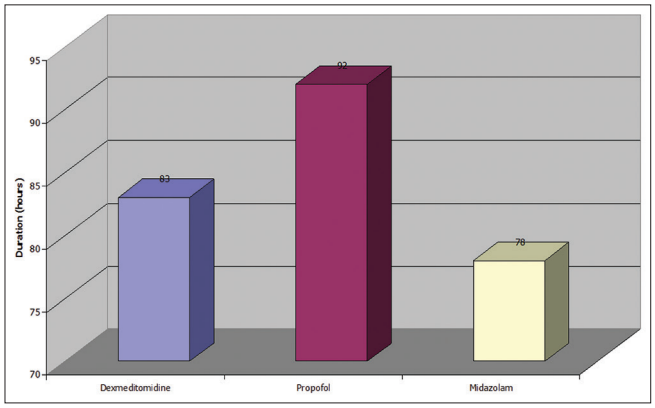

Figure 9: Duration from cessation of sedation to intensive care unit discharge

responses, ventilation and extubation characteristics, and patient perceptions of dexmedetomidine with those of the commonly used i.v. sedative agent propofol and midazolam in the ICU.

On analyzing the demographic data, the three groups were statistically comparable with respect to age, sex, and weight.

The patients in this study were of gynecological and obstetrical cases, emergency laparotomy cases, trauma cases, post-operative routine cases, aspiration pneumonia cases, and COPD cases.

The groups were studied and compared with respect to:

- Duration of sedation ICU length of stay
- Changes in cardiovascular and respiratory status
- Any complications.

In this trail, the use of dexmedetomidine propofol and midazolam for sedation in patients in the ICU was associated with reduced time to tracheal extubation for dexmedetomidine (7.4 ± 1.85) h, for propofol (5.6 ± 1.56) h compared to midazolam (16.9 ± 15. 62) h.

P value between dexmedetomidine and propofol group is >0.05 which is statistically not significant.

P value between dexmedetomidine and midazolam group is <0.001 which is highly significant. *P* value between propofol and midazolam group is <0.00l which is patients on dexmedetomidine and propofol having shorter extubation times than with the midazolam. Study done by Anger *et al.*[1] concluded that management of pain and sedation therapy is a vital component of optimizing patient outcomes; we sought to evaluate efficacy and safety outcomes between post-operative mechanically ventilated cardiac surgery patients receiving dexmedetomidine versus propofol therapy on arrival to the ICU. No differences in the ICU length of stay and duration of mechanical ventilation were seen between the propofol and dexmedetomidine groups, respectively. Reichert *et al.*[2] concluded that no statistically significant differences were noted between the propofol and dexmedetomidine groups when assessing the outcomes of opioid requirements and the time to extubation, above-mentioned both studies shows that no significant difference in the time to extubation after stoppage of sedation as this is also the finding of our study that there was no significant difference in the time to extubation. Aitkenhead *et al.*[3] concluded that desired level of sedation was achieved easily in most patients in both groups. There were slight falls in arterial pressure, but there were no significant differences between the groups. Heart rate (HR) was lower in patients who received propofol. When the infusion was discontinued, there was less variability, in recovery of consciousness in patients who had received propofol. In a subgroup of patients, weaning from mechanical ventilation was achieved significantly faster after discontinuation of propofol than of midazolam. Grounds *et al.*[4] concluded that propofol infusion allowed rapid and accurate control of the level of sedation which was satisfactory for longer than with midazolam, patients given propofol recovered significantly more rapidly from their sedation once they had fulfilled the criteria for weaning from artificial ventilation and as a result spent a significantly shorter time attached to a ventilator. There were no serious complications in either group. This study is in accordance to our study in which we found that significant difference is present in weaning the patient from mechanical ventilator after stoppage of sedation. Midazolam took longer time in weaning.

In our study, we found that patients receiving dexmedetomidine have significantly lower HR compare to propofol and midazolam, during sedation mean pulse rate in dexmedetomidine group was 77.54 ± 9.34, in propofol group 89.34 ± 10.1 and for midazolam group 90.23 ± 10.7.

During sedation with dexmedetomidine, propofol and midazolam $P < 0.001$ which is highly significant.

Hence, its clearly showed in our study that dexmedetomidine infusion leads to reduction in HR during sedation an it is statistically significant when compared with propofol and midazolam. Hoy and Keating[5] concluded that intravenous dexmedetomidine is generally well tolerated when utilized in mechanically ventilated patients in an intensive care setting and for procedural sedation in non-intubated patients. While dexmedetomidine is associated with hypotension and bradycardia, both usually resolve without intervention. Eren and Cukurova[6] concluded that dexmedetomidine was as effective as higher doses of midazolam in sedation. The hemodynamic and respiratory effects were minimal. Although dexmedetomidine caused significant decrease in the BP and HR, it probably just normalized increased levels caused by preoperative stress. Venn *et al*.[7] who demonstrated statistically significant reduction in pulse rate in patients receiving dexmedetomidine infusion in the ICU. After discontinuation of sedation HR was initially lower in patients receiving dexmedetomidine, but after a return to baseline in these patients, there was no difference among the groups ($P \sim 0.15$).

All of the above studies showing that dexmedetomidine infusion leads to reduction is HR which is in accordance to our study which also shows that patients receiving dexmedetomidine infusion having lower HR.

In our study during the sedation with dexmedetomidine, propofol and midazolam there was no significant effect on respiratory rate was noted ($P > 0.05$). Hoy and Keating[5] concluded that intravenous dexmedetomidine is generally well tolerated when utilized in mechanically ventilated patients in an intensive care setting and for procedural sedation in non-intubated patients. It is not associated with respiratory depression.

Arain and Ebert[8] concluded that during sedation with dexmedetomidine and propofol; there was hemodynamic variables (HR and mean arterial BP), sedation, bispectral index score of sedation, ventilation (respiratory rate, O_2 sat, and $ETCO_2$) were determined during surgery and up to 95 min after surgery. Intraoperative sedation levels were targeted to achieve a bispectral index score of 70-80; patient baseline cardiorespiratory variables were similar between groups. There were no differences between groups in psychomotor performance and respiratory rate during recovery. Hence, this study also supports our outcome that dexmedetomidine and propofol not significantly affect respiratory rate during and after sedation in the period of recovery. Hsu and Cortinet (2004) concluded that dexmedetomidine infusions (1) did not result in clinically significant respiratory depression, (2) decreased rather than increased the apnea/hypopnea index, and (3) exhibited some similarity with natural sleep.

Arterial pressures were reduced in dexmedetomidine, propofol, and midazolam sedation. The difference in arterial pressure between all the three groups during sedation was found to be statistically not significant ($P > 0.05$). Stephan and Sountag propofol alone decreased mean arterial pressure and cardiac index; HR was increased. Myocardial blood flow and myocardial oxygen consumption were decreased by 26% and 31%, respectively. This result is in accordance of our study where arterial pressure reduced during propofol sedation. Ebert *et al*.[9] propofol infusions significantly lowered sympathetic nerve activity and BP and increased HR. Cardiac baroreceptor sensitivity determined during nitroprusside was reduced 60% during propofol infusions. The above-mentioned studies show that there is reduction in arterial pressure after propofol sedation which our study also showed. Hence, our study is in accordance to the studies above. Sunzel and Paalzow concluded that a maximal reduction of BP and $PaCO_2$ was produced after sedative doses of midazolam and diazepam. A possible acute tolerance development toward the BP reduction was found after the repeated administration of diazepam but not after the midazolam administration. The plasma concentrations producing half the maximal effects after administration of midazolam was 50-60 ng/ml, indicating that the influence on BP and $PaCO_2$ after drug administration is evoked at lower plasma concentrations than sedation. Lebowltz *et al*., midazolam was associated with more gradual and less pronounced hemodynamic alteration; the only significant changes from baseline were decreases in mean arterial pressure 5 and 10 min after injection. In our study, we found that there was reduction in arterial pressure during midazolam sedation this finding is in accordance of both the studies mentioned above where the investigator found that there was reduction in arterial pressure so his findings support our observation. Ebert *et al*.[9] concluded that dexmedetomidine decreased catecholamines 45-76% and eliminated the norepinephrine increase. Catecholamine suppression persisted in subsequent infusions. The first two doses of dexmedetomidine increased sedation 38 and 65%, and lowered mean arterial pressure by 13%, but did not change central venous pressure or pulmonary artery pressure. Rogue *et al*. (2002) concluded that plasma norepinephrine concentrations, BP, HR, and some HR variability measures were lower after 1 h infusion of dexmedetomidine. Thus, the above-mentioned studies show that there is fall in BP with dexmedetomidine, propofol, and midazolam which is in accordance to our study in which fan of BP was present with all the three drugs.

The mean SpO_2 in all the three groups during sedation, from cessation of sedation to extubation at extubation and from extubation to ICU discharge, were comparable

in dexmedetomidine, propofol, and midazolam groups and there was statistically significant difference found ($P > 0.05$).

Complications

In this study, chest complications (nosocomial pneumonia, barotraumas) were the most common complication noted. 18% patients in dexmedetomidine groups, 25.4% patients in propofol group, 21% patients in midazolam group had chest complications. These findings were in accordance to Goodman *et al*.[10] who studied the ventilatory effects of propofol infusion and concluded that it leads to more chest complications.

Ventricular tachycardia (6.89%) occurred only in propofol group. This finding was in accordance with King *et al*. who showed that propofol infusion leads to acute cardiac failure, cardiomyopathy, and other cardiac complications.

Bradycardia occurred in 7.5% patients receiving dexmedetomidine and the time of loading of the drug. This finding was in accordance with Eren and Cukurova[6] who showed that dexmedetomidine cause bradycardia.

Intravenous line sepsis occurs more frequently with propofol 11.2% as compared to midazolam 8.9% and dexmedetomidine 7.3%.

Prolonged sedation after cessation of sedation occurred most frequently with midazolam 11.34% than with propofol 3.11% and not seen in dexmedetomidine group. This finding in accordance with study done by Slark *et al*., in which he found that patients receiving midazolam lead to prolonged sedation.

Hypotension occurred 14.22% in propofol group, 6.4% in dexmedetomidine group, and 5% in midazolam group. More hypotension in propofol group is in accordance to study done by Larsen *et al*.

None of the complications were statistically significant.

CONCLUSION

Dexmedetomidine a new sedative-analgesic agent is safe to be used in the ICU. Dexmedetomidine provides hemodynamic stability and has no clinically important adverse effects on respiration. Tracheal extubation was earlier in patients receiving, dexmedetomidine and propofol than from midazolam.

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Original Article

Role of Routine Ultrasound in First Trimester of Pregnancy: A Descriptive Study

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Abstract

Introduction: First trimester of pregnancy is a period of rapid development where embryo attains a human form and ultrasound is a very sensitive method of evaluating early pregnancy. Routine ultrasound between 8 and 12 weeks of gestation helps in identification of many physiological and pathological problems and the timely interventions and management. Inspite of this, even today in developing/industrialized countries, this is not being routinely done.

Aim: To emphasize the need for routine ultrasound in first trimester of pregnancy for detection of early gestation, its viability and also early detection of complications by sonoembryology.

Methods: This study is a descriptive study involving 100 low-risk pregnant women between 8 to 12 weeks of gestation with known last menstrual period conducted at Subharti medical college meerut. All the patients were subjected to transabdominal sonography (TAS) and followed by transvaginal sonography (TVS) and were followed till delivery with subsequent scan when necessary.

Results: A total of 100 pregnancies were intrauterine of which 3 were an embryonic and 4 had early pregnancy failure, 13 pregnancies were redated, one subchorionic leave separation, 3 physiological herniation of bowel loops, and 1 physiological herniation with single cord cyst were identified only by TVS and had favorable outcome. Two twin pregnancies were identified and managed.

Conclusions: The study showed the routine ultrasound in first trimester in low-risk women was helpful in timely identification of complications and redating of the pregnancies, thereby reducing the induction rates. This study also gives insight that TVS is superior to TAS in evaluation of fetal structure.

Key words: Ultrasound, First Trimester, Pregnancy

INTRODUCTION

Ultrasound is a very sensitive method of evaluation in early pregnancy. The advent of ultrasound has made an indisputable impact on assessment of clinical condition in the first trimester.[1]

The first trimester of pregnancy is a period of rapid change that spans fertilization of formation of the blastocyst, implantation, gastrulation, neurulation, the embryonic period (6-10 weeks), and early fetal life.[2] By 5 weeks of gestation, ultrasound can usually identify the location and viability of pregnancy as well as gestational age.[3] Apart from pregnancy, uterine anomalies, adnexal pathologies, and cervical length can be detected accurately in the first trimester of pregnancy. Furthermore, all the first trimester complications can be identified earlier even before they manifest clinically. Antenatal detection of fetal malformations has shown to reduce maternal and perinatal morbidity and mortality by allowing elective termination of malformed fetus.[4]

Prenatal screening of down's syndrome[5] and other aneuploidies[6] using ultrasound measurement of fetal nuchal translucency (NT) in combination with other sonographic soft markers and serum markers are found to be very sensitive, hence offers better antenatal care.

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Aims and Objectives

To emphasize the need for routine ultrasound in first trimester of pregnancy for detection of early gestation, its viability, and also early detection of complications by sonoembryology.

MATERIALS AND METHODS

This descriptive study involved low-risk 100 pregnant women between 8 and 12 weeks of gestation with reliable last menstrual period (LMP) details and attending antenatal clinic at Subharti medical college meerut, during the period of 2 years from December 2007 to December 2009. Purposive sampling was done.

Inclusion Criteria

Pregnant women with history of amenorrhea >8 weeks and <12 weeks of gestation.

Exclusion Criteria

- Individuals with history of pain abdomen and bleeding per vaginam.
- Individuals with history of previous abortions.
- Elderly primigravida.
- Uterine anomalies.

After informed written consent, detailed history, thorough clinical examination was made at booking. All routine first trimester investigations were carried out according to the hospital protocols. All patients were subjected to transabdominal sonography (TAS) and transvaginal sonography (TVS) after explaining the procedure to the patient. All cases were followed up till the delivery with subsequent scan done when necessary. Our institution is registered under PNDT act and has followed the rules and regulations according to the act.

Study parameter considered are gestational sac shape, number and location, yolk sac size and shape, presence or absence of fetal pole, cardiac pulsation absent or present, crown-rump length (CRL) measurements, uterine anomalies and tumors, presence of corpus luteum, pelvic or adnexal mass, cervical length, study of nuchal translucency (NT) and nasal bone.

Statistical Methods

Descriptive statistical analysis with categorical measurements is presented in numbers (%) or mean±standard deviation. Chi-square/fisher exact test was used to find the significance of study parameters.

Analysis of variance formula and statistical software SPSS 15.0, Stat 8.0 were used for the analysis for the data.

RESULTS

Descriptive study involved in 100 pregnant women between 8 and 12 weeks of gestation with 57% of the women aged between 20 and 24 years and 37% between 25 and 29 years and 62% were primigravida and 38% were multigravida. All patients belong to low risk at the time of booking.

DISCUSSION

The antenatal care is the preventive and prophylactic arm of obstetric practice and ultrasound is an integral part of this antenatal care.

Ultrasound when employed in first trimester can accurately date the pregnancy and by this induction rates can be reduced by 40%.[7]

In this descriptive study, 100 pregnant women between 8 and 12 weeks of gestation were involved. The majority of the women were between 20 and 24 years and 62% of them were primigravidae with known LMPs. None of the 100 women had any first trimester complaints, previous history of recurrent abortions, uterine anomalies or medical disorders. They belonged to a low-risk population and majorities were screened between 9 and 9.9 weeks (Table 1). All the 100 women underwent transabdominal scan followed by transvaginal scan.

Out of the 100 pregnant women scanned, anembryonic pregnancy found to be 3%, which correlates with many other studies (Table 2).[8-11]

The difference between gestation age by dates and by scan was found to be >5 days in 13 women, i.e., 13.4%. The number of pregnancies redated was 13.4% and a significant reduction in induction rate was 46%. Wide variation is noted in different studies in date reassignment, which

Table 1: Gestational age distribution

Gestational age by dates (in weeks)	Number *n*=100 (%)
8-8.9	24 (24)
9-9.9	32 (32)
10-10.9	9 (9)
11-11.9	18 (18)
12	17 (17)

Table 2: Fetal pole

Fetal pole	Number *n*=100 (%)
Absent	3 (3)
Present	97 (97)

varies from 5.7% to 40%.[12,13] Three were anembryonic pregnancies, hence CRL was not done and fetal heart rate (FHR) was identified in 93 patients with 4 cases showing early fetal demise (Table 3).

Gestational sac was found to be normal with respect to its location and shape suggesting intrauterine pregnancies in all the cases. The mean yolk sac values increased as the gestational age increased (Table 4). Yolk sac shape and echolucency was found to be normal in all the cases.

Cervical length measurement was done for all the patients and found that no statistical difference in the measurement by TAS and TVS with $P > 0.05$ and mean cervical length being 36.40 mm (TAS) and 37.71 mm (TVS), respectively.

Two twin pregnancies were diagnosed, but TAS could identify only 1 among the 2. Physiological herniation of bowel loops was observed in 4 pregnancies all only by TVS suggesting statistical significance with p value of 0.043 compared to TAS (Table 5).

Of the 100 pregnancies, 22 of them were abnormal, i.e., blighted ovum constituted 3%, early embryonic demise 4%, subchorionic leave separation 1%, wrong dates 13% and physiological herniation of bowel loop with a single umbilical cyst was 1%. 7 pregnancies were electively terminated and the rest had favorable outcome (Table 6).

In 58 pregnant women, NT was not measured as the period of gestation was <11 weeks, but were followed up subsequently. Rest of them was measured and was found to below the 95th percentile with respect to CRL values (Table 7).

Of the 100 pregnancies, 22 were found to be abnormal at the end of the first trimester scan.

Ultrasound is a reliable method to identify nonviable pregnancies before the clinical manifestation, hence enables planned termination avoiding emergency surgery and physical trauma of unexpected vaginal bleeding.

Ultrasound also accurately dates the pregnancy, reducing the induction rate, and identifies the multiple pregnancies and chorionicity accurately.

Accurate NT measurement is a reliable method of screening for fetal abnormalities; also some structural abnormalities can be identified earlier with visualization of the uterus and adnexal structures and cervical length.

Summary

This is a descriptive study of 100 pregnant women between 8 and 12 weeks of gestation attending ANC at Subharti Medical College, Meerut and study conducted between December 2007 and December 2009. All patients after meeting the inclusion criteria were subjected to TAS and TVS and were followed till delivery. Different statistical analysis was applied using descriptive statistics.

Majority in this study were screened between 9 and 9.9 weeks of gestation and all were intrauterine pregnancies. 3% of pregnancies were anembryonic, 4% showed early fetal demise, 13.42% were redated and followed up. Overall 8 complications were identified, majority were by TVS. There was correlation between TAS and TVS with respect to cervical length, yolk sac measurement.

Thus routine ultrasound in first trimester was a reliable method to date pregnancy, identify nonviable pregnancies and early trimester complications. It is also a noninvasive method of identifying fetal abnormalities at the earliest, thereby enabling early termination of pregnancy. Hence, it should be offered to all patients.

Table 3: Gestational age and CRL

Gestational age by scan (in weeks)	Number (*n*=97)	Mean±SD
6-6.9	2	13.85±0.21
7-7.9	2	15.20±1.70
8-8.9	30	20.41±4.07
9-9.9	23	27.69±2.81
10-10.9	6	35.28±2.7
11-11.9	12	47.05±8.86
12-12.9	18	55.64±2.67
13-13.9	2	66±0
14-14.9	2	86.2±0
Total	97	34.27±15.94

CRL: Crown rump length, SD: Standard deviation

Table 4: Yolk sac measurements

Method of scan	Mean yolk sac measurement (mm)	Mean±SD	*t*	*P*
Transabdominal	3.46	1.02±0.016	0.11	0.915
Transvaginal	3.48	1.00±0.016		

SD: Standard deviation

Table 5: Findings of transabdominal scan and transvaginal scan

Method of scan	Number	Gestational sac		Physiological herniation of bowel loops (%)	Complications (%)
		Single (%)	Double (%)		
Transabdominal	100	99 (99)	1 (1)	0	7 (7)
Transvaginal	100	98 (98)	2 (2)	4 (4)	8 (8)

Table 6: Findings of scan

Findings of scan	Number *n*=100 (%)
Normal	78 (78)
Abnormal	22 (22)
Herniation of bowel loops with single cord cyst	1 (1)
Blighted ovum	3 (3)
Embryonic demise	4 (4)
Wrong dates	13 (13)
Subchorionic leave separation	1 (1)

Table 7: Nuchal translucency

Nuchal translucency (mm)	Number *n*=93 (%)
Not measured	58 (62.36)
0.1-1.0	18 (19.35)
1.1-2.0	17 (18.27)

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Original Article

Estimation of Perioperative Serum Potassium Levels and Cardiovascular Changes during Laparoscopic Surgery: An Observational Study

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Abstract

Background: Laparoscopic surgeries are preferred and are becoming a standard therapeutic procedure. CO_2 insufflation in these surgeries results in hemodynamic changes and fluctuations in the potassium level.

Materials and Methods: The observational study was conducted in Department of Anaesthesia in Teerthanker Mahaveer Medical College and Research Centre on 100 patients undergoing laparoscopic surgery. Blood potassium level and hemodynamic parameters (pulse rate, systolic, and diastolic blood pressure) were measured at four stages of surgery (preinduction, pre-insufflation, immediate postexsufflation, and immediately after extubation) were recorded. The results were analyzed by Students "*t*" test and $P < 0.01$ was considered as significant.

Results: The changes in potassium level showed a significant difference in postexsufflation stage in which potassium level changed significantly (<0.01). The hemodynamic parameters (pulse rate, systolic, and diastolic blood pressure) showed no significant difference in four stages of surgeries.

Conclusion: This study endorses that checking of serum potassium should be conducted in patients enduring laparoscopic procedures of extended duration.

Key words: Hemodynamic, Laparoscopy, Potassium, Surgery

INTRODUCTION

The laparoscopic procedures which are minimally invasive causes less trauma and are cheaper is the requirement of modern era. Previously, the laparoscopic surgeries were done mainly in cholelithiasis and in gynecological procedures. But now, these surgeries are preferred and are becoming a standard therapeutic procedure.[1,2]

There are a number of advantages to the patient with laparoscopic surgery as compared with the open procedure. Small sized incisions result in the decrease in incidence of pain and hemorrhage. Furthermore, the hospital stay and recovery time are reduced.[3]

The key element in laparoscopic surgery is the use of a laparoscope, a long fiber optic cable system which allows viewing of the affected area by snaking the cable from a more distant, but more easily accessible location.[4]

Although, these surgeries have various benefits but some limitations are present which require thorough research. The biggest disadvantage of such type of surgeries is that CO_2 insufflation in the peritoneal cavity is the essential step which causes increase in intra-abdominal pressure. This results in hemodynamic changes and fluctuations in the potassium level.[5,6]

Literature regarding the effect of CO_2 insufflation is lacking. Various animal studies[1,6,7] have informed life-threatening

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increase in serum potassium levels or hyperkalemia during CO_2 procedures.

Hyperkalemia is defined as an elevated level of potassium in the blood serum. Normal potassium levels are between 3.5 and 5.0 mmol/L. When the rise is severe it results in palpitations, muscle pain, muscle weakness, or numbness. An abnormal heart rate can occur which can result in cardiac arrest and death. Abnormal rise in potassium level can lead to ischemia of the abdominal muscles and intracellular acidosis in abdominal organs due to carbon dioxide diffusion.[8]

With the increasing trend of laparoscopic surgeries, it is now essential for the researchers to study its various aspects. Thus, we conducted this study in our medical college to study the effect of laparoscopic surgeries on potassium level and hemodynamic parameters.

MATERIALS AND METHODS

The observational study was conducted in the Department of Anaesthesia in Teerthanker Mahaveer Medical College and Research Centre on 100 patients undergoing laparoscopic surgery. Detailed history was taken, and complete clinical examination was done. Basic investigations were done.

The intravenous line was secured and connected to monitor NIBP, SPO_2, and electrocardiogram. Hemodynamic parameters before induction were recorded. Furthermore, blood potassium level was measured. The patients were induced by giving thiopentone sodium 5 mg/kg, and orotracheal intubation was facilitated by 0.1 mg/kg of vecuronium bromide. 66% nitrous oxide in oxygen with 0.5-1% isoflurane was used for maintenance of anesthesia. Fentanyl 2 μg/kg was added as analgesic drug. CO_2 insufflation was done, and intra-abdominal pressure of 13 mm of Hg was maintained. Four blood potassium levels were measured (preinduction, pre-insufflation, immediate postexsufflation, and immediately after extubation). The hemodynamic parameters (pulse rate, systolic, and diastolic blood pressure) were recorded. The results were analyzed by Students "*t*" test and $P < 0.01$ was considered as significant.

RESULTS

The study was conducted in patients aged 25-60 years with a male:female ratio of 2:1. All the basic investigations such as serum electrolytes, blood urea, serum creatinine, blood sugar, serum bilirubin, and hemoglobin were in normal range. Preinduction values of various parameters were noted and taken as baseline values for the purpose of evaluation with consequent values of the identical parameters.

The pre-induction value of serum potassium level was 4.125 ± 0.31 meq/L. The changes in potassium level in different phases of surgery showed no significant difference except postexsufflation stage in which potassium level changed significantly (<0.01) to 4.854 ± 0.51 (Table 1 and Figure 1).

The mean systolic blood pressure in different stages of surgery when compared with preinduction period did not show any significant increase or decrease throughout the procedure. No patient showed abnormal deviation from the mean values during the study period (Table 2 and Figure 2).

No statistically significant change in mean blood pressure was found during insufflation of carbon dioxide and throughout the procedure ($P > 0.01$) at all intervals. No individual abnormal variation in diastolic blood pressure was noted (Table 3 and Figure 3).

The changes in pulse rate during different periods when compared with the baseline values were statistically insignificant ($P > 0.01$). No rhythm disturbance except transient sinus tachycardia at the time of intubation and extubation were observed (Table 4 and Figure 4).

Table 1: Variations in serum potassium (meq/L) during laparoscopic surgery

Phase	Mean±standard deviation	*t* value	*P* value
Preinduction	4.125±0.31	-	-
Pre-insufflation	3.912±0.293	0.49	≥0.01
Postexsufflation	4.854±0.51	4.133	0.006
Postextubation	3.64±0.358	2.49	≥0.01

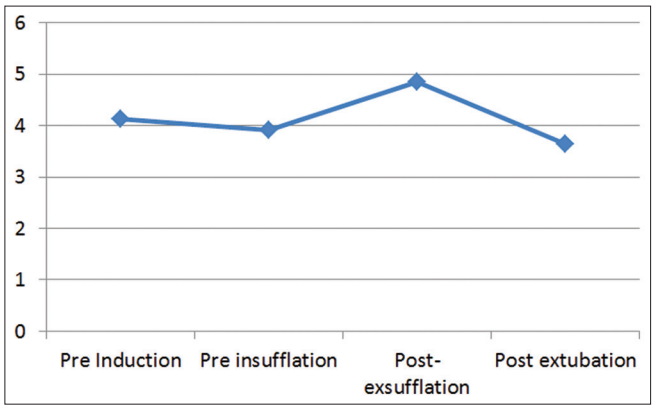

Figure 1: The changes in serum potassium level in different phases of surgery

Table 2: Variation in systolic blood pressure (mm of Hg) during laparoscopic surgery

Phase	Mean±standard deviation	*t* value	*P* value
Preinduction	124.20±11.26	-	-
Pre-insufflation	120.32±15.22	1.68	≥0.01
Postexsufflation	128.2±17.6	0.85	≥0.01
Postextubation	135.04±15.4	1.28	≥0.01

Table 3: Variation in diastolic blood pressure (mm of Hg) during laparoscopic surgery

Phase	Mean±standard deviation	*t* value	*P* value
Preinduction	62.00±8.48	-	-
Pre-insufflation	56.00±6.8	1.86	≥0.01
Postexsufflation	54.00±7.4	0.95	≥0.01
Postextubation	59.00±8.5	1.49	≥0.05

Table 4: Variation in pulse rate per minute during laparoscopic surgery

Phase	Mean±standard deviation	*t* value	*P* value
Preinduction	80.1±7.11	-	-
Pre-insufflation	83.41±7.58	1.82	≥0.01
Postexsufflation	78.50±6.44	0.74	≥0.01
Postextubation	84.22±7.81	0.88	≥0.01

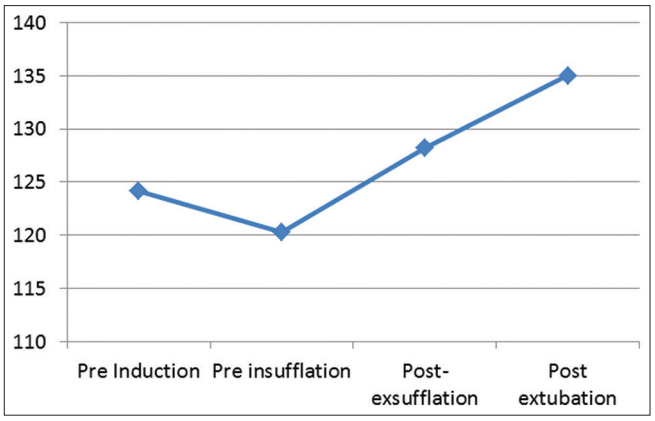

Figure 2: The changes in systolic blood pressure in different phases of surgery

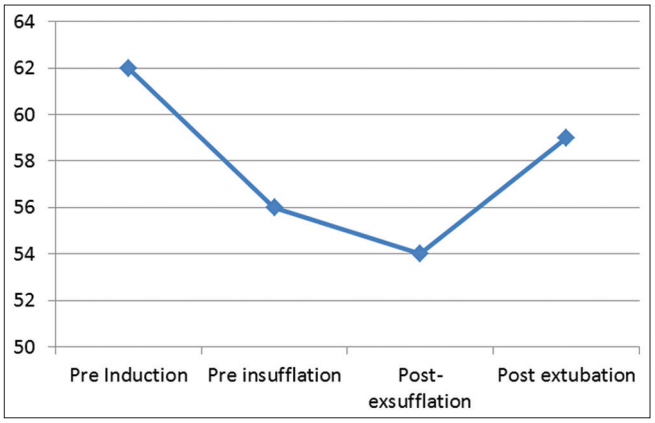

Figure 3: The changes in diastolic blood pressure in different phases of surgery

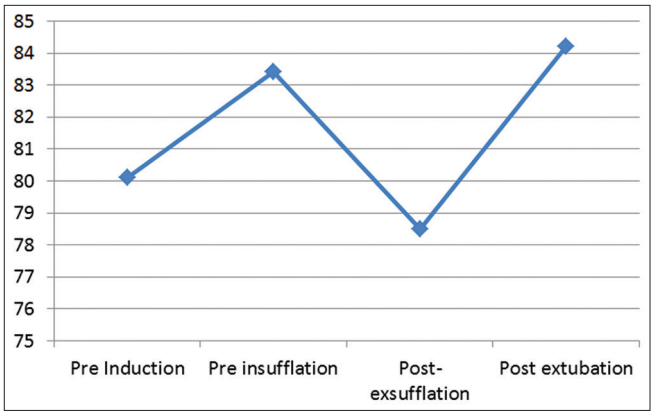

Figure 4: The changes in pulse rate in different phases of surgery

DISCUSSION

Laparoscopic surgery has become the new gold standard for the treatment of various diseases in the modern era. First laparoscopic surgery was performed by French surgeon Philippe Mouret in 1987. Laparoscopic surgery is preferred technique because it includes less pain, invisible scar, earlier return to work, a satisfied patient, less financial burden, etc.[9]

In this study, an attempt was made to evaluate any change in potassium levels and hemodynamic changes in patients undergoing laparoscopic surgery especially during carbon dioxide insufflation, a step toward identifying the possibility of such contingency in explaining the cause of manifestation of unexplained dysrhythmias during the process.

The literature regarding the variations in serum potassium level in laparoscopic surgeries is lacking. Various studies on animals have been done. In an animal study, Diamant et al.,[10] pigs were subjected to 3.5 h of carbon dioxide pneumoperitoneum, the mean rise of potassium was 5.63 (standard deviation 0.44) which was statistically significant and clinically life threatening. This verdict, though not quantitatively of equal scale, yet allied to this study. The feasible reason could be a minor time of carbon dioxide pneumoperitoneum in our study. The various mechanisms to elevate serum potassium could be tissue damage, ischemia, decreased perfusion of abdominal muscles due to stretching, renal hypoperfusion, alteration in hydrogen ion concentration, and possibly intracellular acidosis due to carbon dioxide diffusion into the cells.

Various study[4,8,11] on hemodynamic changes during laparoscopic cholecystectomy with intra-abdominal

pressure between 13 and 15 mm of Hg have shown a cardiac output either unchanged or modestly increased. When arterial carbon dioxide tension and intra-abdominal pressure are kept within physiological acceptable limits, hemodynamic parameters, i.e., pulse rate and blood pressure do not change significantly. Like most modern sets, intra-abdominal pressure was maintained at 13 mm of Hg, and no hemodynamic alteration of clinical importance was observed in any of the patients, except for the usual intubation and extubation responses.

Slight fall in blood pressure was probably due to induction with thiopentone. The fall in the blood pressure is often accompanied by slight tachycardia and has been attributed to vasodilation, peripheral pooling of the blood, and consequent decrease in venous return.[4] The negative findings of hemodynamic changes can be attributed to the patients at risk for such events were excluded from the study, absence of major hemodynamic alteration, the potassium levels despite significant increase, remained well within normal limits, and the relatively short duration (40 min) of carbon dioxide insufflation.[9]

CONCLUSION

This study endorses that checking of serum potassium should be conducted in patients enduring laparoscopic procedures of extended duration. It is recommended that potassium level estimation is essential in patients with high risk of hyperkalemia as it can lead to development of arrhythmia.

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Original Article

Morbidity and Mortality Patterns in Small for Gestational Age versus Appropriate for Gestational Age Preterm Neonates Admitted in Level II Neonatal Intensive Care Unit: A Observational Study

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Abstract

Introduction: Preterm birth is a significant public health problem across the world because of associated neonatal (first 28 days of life) mortality and short- and long-term morbidity and disability in later life. Currently, prematurity is the leading cause of death among children under five around the world, and a leading cause of disability and ill health later in life.

Objective: To study and compare the morbidity and mortality patterns in preterm small for gestational age (SGA) babies in relation to preterm appropriate for gestational age (AGA) babies admitted to level II Neonatal Intensive Care Unit (NICU) in Niloufer Hospital.

Methods: An observational retrospective study was conducted in level II NICU in Niloufer Hospital. The study was conducted for a 6 month period. Neonates born with a weight of <1.5 kg were included in the study. Data regarding morbidities and demographic parameters were obtained from the casesheets of the admitted neonates. The data obtained was analyzed using IBM SPSS statistics version 19.0 and $P < 0.05$ was considered statistically significant.

Results: A total of 95 babies were studied. The risk of respiratory distress syndrome (RDS) was lower in SGA babies compared to AGA babies. SGA babies had more risk of hypoglycemia and sepsis compared to AGA babies. The duration of hospital stay and mortality was also more in SGA babies compared to AGA babies. The most common morbidity was neonatal jaundice followed by RDS. The extremely low birth weight (ELBW) group had higher rates of all the morbidities. The morbidities were also commoner in lower gestational ages.

Conclusion: SGA neonates have high morbidities and mortality rate compared to AGA neonates. The mortality and morbidities are higher in ELBW and at lower gestational ages. The prognosis of these babies can further be improved by antenatal steroids to eligible pregnant with risk of preterm delivery. The inclusion of prenatal education and screening for medical disorders in antenatal care guidelines will help in curtailing the incidence of preterm deliveries.

Key words: Appropriate for gestational age, Morbidity, Mortality, Preterm neonates, SGA

INTRODUCTION

Preterm birth is a significant public health problem across the world because of associated neonatal (first 28 days of life) mortality and short- and long-term morbidity and disability in later life. Currently, prematurity is the leading cause of death among children under five around the world, and a leading cause of disability and ill health later in life.

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An estimated 20 million infants every year are born with low birth weight (LBW; <2500 g)[1] and these infants have an increased risk mortality in the first year of life. The primary causes of LBW are preterm birth, intrauterine growth restriction (IUGR), or a combination of the two. Of 135 million children born in low-income and middle-income countries (LMICs) in 2010, an estimated 29.7 million

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were born both term and small for gestational age (SGA), 10.9 million were born preterm and appropriate for gestational age (AGA), and 2.8 million were born preterm and SGA.[2] Risk factors and interventions to reduce the number of babies born SGA might differ from those to reduce the number of babies born preterm. Few studies in LMICs have investigated differences in mortality by extent of prematurity, IUGR, or the two in combination.[3,4] Examination of the mortality risk by degree of prematurity and SGA as a proxy for IUGR might be crucial in understanding the attributable disease burden, because regions such as South Asia have a reported SGA prevalence of about 40%.[5,6] Especially with high incidences for LBW and IUGR-LBW in India (28%, 21%), respectively.[7]

The preterm babies (SGA or AGA) also carry increased risk of neonatal morbidity or complications. These complications include respiratory distress syndrome (RDS), intraventricular hemorrhage (IVH), sepsis, necrotizing enterocolitis (NEC), patent ductus arteriosus (PDA), hyperbilirubinemia, feeding difficulties, temperature instability, hypoglycemia, and hypocalcaemia.[8] Such mortality risk estimates and attributable burden could enable the specific targeting of these disorders with appropriate interventions to more effectively save lives.

This study was conducted to evaluate the mortality and morbidity pattern at level II Neonatal Intensive Care Unit (NICU) in Niloufer Hospital in relation to SGA versus AGA preterm. Once the baby is hemodynamically stable, the mothers are trained to take care of their babies.

MATERIALS AND METHODS

A retrospective observational analysis was conducted at level II NICU, tertiary care center, Niloufer Hospital, Hyderabad, to study and compare the morbidity and mortality pattern in SGA versus AGA preterm. Retrospectively babies admitted in the 6 months period from January to June 2015 were included in the study. We included intramural and extramural neonates born to singleton mothers with gestation age <37 weeks and birth weight <1.5 kg. Birth weight below 10th centile was defined as SGA neonates and between 10th and 90th centile as AGA neonates on Fenton charts used in our hospital. We excluded infants with major malformations.

Case records of neonates were scrutinized for antenatal and postnatal data. The demographic parameters and morbidities were collected in a predesigned pro forma. The morbidities included were RDS, apnea of prematurity, NEC, PDA, hypoglycemia, hypocalcemia, sepsis, requirement of higher antibiotics, intracerebral hemorrhage (ICH)/IVH, anemia, neonatal jaundice (NNJ), etc., were studied and a comparison of the morbidities was made between birth weight and gestational age among SGA and AGA babies.

Data were analyzed using SPSS statistics version 19.0. For descriptive statistics, frequencies were tabulated and Chi-square test was done to see significance between the groups. A $P < 0.05$ was considered statistically significant.

RESULTS

A total of 95 neonates were enrolled in the study. Of these 47 (48.5%) were males and 48 (49.5%) were females. Inborn babies were 24 (24.7%) and outborn were 71 (73.2%). Mean birth weight 1205.29 g (±180.8g) and mean gestation age 30.92 weeks (±2.3 weeks). Extremely LBW (ELBW) (<1000 g) constituted 15 (15.6%) and very LBW (VLBW) (1000-1499 g) 80 (84.3%) neonates. Proportion of babies who were SGA was 46 (48.4%) and AGA 49 (51.6%). 37 babies (38.5%) were delivered by LSCS and 58 babies (60.4%) were delivered by vaginal route. The underlying cause of prematurity in the majority of the cases was pregnancy induced hypertension (26.31%).

Only 6 (6.3%) babies received complete course of antenatal steroids.

The morbidities of neonates based on weight with respect to AGA/SGA are as follows (Table 1).

RDS, hypoglycemia, NEC, and sepsis were statistically significant among the SGA and AGA groups

Table 1: Morbidities/mortality among SGA in relation to AGA preterm

Variables	SGA *n*=46 (%)	AGA *n*=49 (%)	*P* value
RDS†	30 (65.2)	43 (87.8)	0.009*
CPAP	5 (10.9)	12 (24.5)	0.071
Mech vent	3 (6.5)	8 (16.3)	0.120
AOP	17 (37)	19 (38.8)	0.512
ICH/IVH	8 (17.4)	9 (18.4)	0.558
NEC	3 (6.5)	1 (2.04)	0.007*
PDA	4 (8.7)	8 (16.3)	0.210
Hypoglycemia*	12 (26.1)	4 (8.2)	0.019*
Hypocalcemia**	3 (6.5)	6 (12.2)	0.276
Sepsis‡	27 (58.7)	17 (34.7)	0.016*
Higher antibiotics	32 (69.6)	38 (77.6)	0.288
Anemia***	7 (14.8)	8 (16.3)	0.553
NNJ	40 (87)	44 (89.8)	0.455
Mean hospital stay	18.04 days	16.73 days	
Deaths	3 (6.5)	1 (2.04)	0.007

*Depicts statistically significant with *P*<0.05, *Random blood glucose level <45 mg/dl, **Total serum calcium level <7 mg/dl, ***Hb<9 g/l, †Signs of respiratory distress developing within 6 h of birth and/or radiological evidence, ‡Based on septic screen/positive blood culture. SGA: Small for gestational age, AGA: Appropriate for gestational age, NNJ: Neonatal jaundice, IVH: Intraventricular hemorrhage, PDA: Patent ductus arteriosus, ICH: Intracerebral hemorrhage

(65.2% vs. 87.8%), (26.1% vs. 8.2%), (6.5% vs. 2.04%), and (58.7% vs. 34.7%), respectively. The difference in the rates of other morbidities was not statistically significant. NNJ 84 (88.4%) was the most common morbidity in preterm followed by RDS 73 (76.8%). The duration of hospital stay was higher in SGA babies compared to AGA babies (18.04 vs. 16.73 days, respectively). The mortality trends for the "very preterm babies" are presented in Table 1. Considering the outcomes, the overall mortality for the "preterm babies" included in the study was 4 (4.2%). There was a significantly lower mortality in the "AGA group as compared to 'SGA group' (2.04% vs. 6.5%, respectively)". Two of the 15 ELBW neonates required LASER for ROP and none of the VLBW babies required treatment for ROP. Two in ELBW group and one in VLBW group did not pass the otoacoustic emissions test and were further advised to do brainstem evoked response audiometry.

All the babies in the ELBW group (100%) and 3/4th of babies in the VLBW group (74.7%) developed RDS. ELBW babies required more C-pap support compared to VLBW babies which was statistically significant (74.6 vs. 35.6%, respectively). The risk of all the morbidities was noted to be higher in ELBW group than in the VLBW group, but the difference was statistically significant only for hypoglycemia, hypocalcemia, sepsis, ICH/IVH, and requirement of higher antibiotics (50 vs. 13.8%, 37.5 vs. 6.9%, 87.5 vs. 42.5%, 62.5 vs. 13.8%, 62.5 vs. 23.0%, respectively). The difference in deaths (20% in ELBW and 5% in VLBW) was also statistically significant. Babies with gestational age <28 weeks had more risk of all the morbidities. Those with gestational age >34 weeks had lesser risk of all the morbidities.

DISCUSSION

Our study showed that the risk of neonatal mortality was highest among preterm SGA compared to AGA babies. However, different studies presented conflicting reports on the outcomes of the prematurity in the SGA and AGA newborns. While some studies reported increased mortality and morbidity rates in the SGA preterm neonates,[9,10] a number of other studies demonstrated decreased rates in this regard.[11] Furthermore, there are several studies reporting no changes in the mortality and morbidity of the preterm SGA neonates, compared to their AGA peers.[12,13]

As the findings of the current study indicated, RDS was less prevalent in the SGA neonates, compared to the AGA ones. These findings are consistent with those observed in some of the previous studies.[11] The most common morbidity in the patients in this study was jaundice followed by respiratory problems which were similar to previous studies.[14-16] Sepsis was also reported[14,17] as one of the common morbidities blood calcium and glucose levels were significantly low in SGA than AGA babies, a finding again similar to those reported by Kramer *et al.*[18] These complications could potentially be prevented, or minimized, with interventions such as Kangaroo Mother Care and extra-support for feeding, case management of babies with signs of infection, safe oxygen management and supportive care for RDS, hospital care of babies with RDS, use of continuous positive airway pressure (CPAP) and surfactant, or intensive neonatal care.[19]

The limitation of this study was focusing on the short-term morbidity outcomes in the SGA and AGA neonates. Future studies are recommended to investigate the late morbidity outcomes in the SGA and AGA newborns using long-term follow-ups. Finally, this is a hospital-based study, and the population coming to this tertiary referral hospital may not be representative of the larger population. However, the objective of this paper was to assess the pattern of morbidities/mortality of the level II NICU care in a tertiary hospital setting so that in the future, the quality of care provided for these infants can be improved.

CONCLUSION

This study is one of very few research studies on this topic from developing countries. More than three-quarters of preterm/premature babies can be saved with often inexpensive care such as good antenatal care, antenatal steroid injections, essential care during child birth, increasing use of CPAP, aseptic precautions during hospital stay, improving breast feeding rates, involving mothers in the neonatal care, and kangaroo mother care. Identification of risk factors in women with improved care before, between and during pregnancies; better access to contraceptives and increased empowerment/education can further decrease the preterm birth rate.

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Original Article

Acute Kidney Injury According to Modified Pediatric Risk, Injury, Failure, Loss, End-Stage Kidney Disease Criteria in the Pediatric Intensive Care Unit: Risk Factors

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Abstract

Background: Acute kidney injury (AKI) classification using Pediatric Modified Risk, Injury, Failure, Loss, End-Stage Kidney Disease (pRIFLE) criteria revealed that AKI is very common in critically ill pediatric patients and is associated with significant morbidity and mortality. Hence, we decided to conduct a study to determine the incidence and risk factors of AKI in pediatric intensive care unit (PICU) patient using pRIFLE criteria.

Materials and Methods: Suspected risk factors for AKI such as age <1 year, weight <10 kg, male gender, pre-existing illness, the pediatric risk of mortality score [PRISM III] (PRISM SCORE) at the day of admission, suspected or proven sepsis, multiorgan dysfunction syndrome, need for ventilator support, duration of ventilation, use of intravenous radiocontrast, use of liposomal amphotericin, use of acyclovir, use of diuretics, use of blood products, and use of noradrenalin were recorded in predesigned assessment sheet. Serum creatinine (estimated creatinine clearance) and urine output were monitored to classify patients into two groups AKI (risk, injury, and failure by modified pRIFLE criteria) and no AKI and then the suspected risk factors were analyzed using univariate and multivariate logistic regression analysis.

Results: Out of 114 patients, 50 patients developed AKI 64 patients (56.2%) did not developed AKI during the study period and served as controls; 23 patients (20.1%) developed pRIFLEmax R AKI; 15 (13.1%) pRIFLEmax I and 12 (10.5%) pRIFLEmax F AKI. Univariate analysis showed that the length of stay in PICU >4 days, PRISM III score >10 and ≥4 days on ventilator support were significant predictors of AKI ($P < 0.01$) whereas multivariate logistic regression analysis showed only the use of diuretics had a protective role in AKI (89.1% vs. 74%, $P = 0.047$, odds ratio of 0.324, and 95% confidence interval: 0.107-0.85), whereas other factors had no role in AKI.

Conclusion: Multidimensional AKI classification and stratification systems, such as pRIFLE, can serve well to improve understanding of AKI epidemiology and potentially optimize evaluation and treatment for AKI in children.

Key words: Acute kidney injury, Modified risk, injury, failure, loss, end-stage kidney disease criteria, Pediatric intensive care unit

INTRODUCTION

The reported mortality from acute kidney injury (AKI) is still as high as 60% in critically ill children.[1] Most of the reported clinical studies of pediatric AKI focus on patients requiring renal replacement therapy, who have clearly experienced severe renal injury.[1] However, recent studies demonstrate that even a modest rise in serum creatinine (SCr) is a risk factor for mortality in adult and pediatric patients.[1,2]

The AKI diagnosis criteria are defined as "an abrupt (within 48 h) reduction in kidney function currently defined as an absolute increase in SCr of more than or equal to 0.3 mg/dL, a percentage increase in SCr of more than or equal to 50% (1.5-fold from baseline), or a reduction in

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urine output (UOP) (documented oliguria of <0.5 ml/kg/h for more than 6 h)."[3] This definition considers the patient's baseline function and changes in clinical markers within a 48-h.

In 2004, the acute dialysis quality initiative proposed a multidimensional AKI classification system in adults termed the Risk, Injury, Failure, Loss, End-Stage Kidney Disease (RIFLE) criteria to promote a consistent AKI definition to compare findings across studies and populations.[4]

AKI plays a major role in the clinical outcomes of critically ill patients. It is estimated that AKI affects approximately 35% of intensive care patients and 4-7% of all hospitalized patients.[5]

Although creatinine level and UOP are not highly sensitive indicators of glomerular filtration rate, they are readily available, clinically tested and verified, and therefore used in most definitions.[6-8]

This study was performed considering the paucity of data available on the incidence and determinants of AKI in Indian children and taking into account the retrospective nature of the previous studies.

Objectives of the Study

To correlate risk factors in children who developed AKI with those who did not develop AKI.

MATERIALS AND METHODS

This was a prospective study that validated pediatric modified RIFLE (pRIFLE) criteria for defining AKI in critically ill children done over a period of 1 year at Narayana Hrudayalaya Multispeciality Hospital, Bengaluru, India. The study was approved by the Institutional Ethics Committee. Informed consent was obtained from the parents before the inclusion of subjects into the study.

Patients aged 1 month to 14 years, admitted to the pediatric intensive care unit (PICU), were eligible for enrollment. Patients with known renal disease and immediately following renal transplantation were excluded. Patients with less than two SCr levels or those with no urine specimens were also excluded from the study. Patients were enrolled within 48 h of admission in the PICU and followed for up to 10 days from enrollment or until PICU discharge.

The clinical variables collected for this study were age, gender, weight, admission and discharge diagnoses, and pre-existing illness: Present/absent, length of stay in PICU, and pediatric risk of mortality score (PRISM III score) (PRISM III, a severity of illness/mortality risk measure) were calculated at the day of PICU admission, need for mechanical ventilation, number of days on mechanical ventilation, use of noradrenalin, use of liposomal amphotericin, antiviral used (acyclovir), use of diuretics, use of intravenous (IV) radiocontrast, use of blood products, sepsis present or absent: Patients were classified as having sepsis if they fulfilled consensus criteria for systemic inflammatory response syndrome, infection, sepsis, and severe sepsis or septic shock suspected or proven (by positive culture, tissue stain, or polymerase chain reaction test) as determined from PICU admission/discharge summaries and laboratory values. Multiorgan dysfunction syndrome (MODS): Presence of >2 altered organ functions such that homeostasis cannot be maintained without medical intervention.

Classification of patients according to pRIFLE criteria (Table 1): Serum Cr values and UOP (in ml/kg/h 8th hourly) were recorded on day 1, 2, 3, 7, and possibly day 10 of PICU stay. Estimated creatinine clearance (eCCl) was calculated using the Schwartz formula (eCCl = K Ht/Sr Creatinine). Patients were classified daily by pRIFLE criteria for AKI, using the changes in eCCl from baseline eCCl and decrease in UOP. The pRIFLE criteria for AKI classified patients' grade of AKI based on changes in eCCl and UOP: pRIFLE R ("Risk") denotes a ≥25% decrease in eCCl or UOP <0.5 ml/kg/h for 8 h; pRIFLE I ("Injury") denotes a ≥50% decrease in eCCl or UOP <0.5 ml/kg/h for 16 h and pRIFLE F ("Failure") denotes a 75% decrease in eCCl from baseline renal function or UOP <0.3 ml/kg/h for 24 h or anuria for 12 h.

The first occurrence of AKI using pRIFLE criteria (based on either UOP or calculated eCCl whichever worst) was noted, and the worst pRIFLE stratum (pRIFLE max) attained in the first 10 days of study enrolment was also recorded.

Patients were classified into two groups AKI and no AKI using modified pRIFLE criteria and risk factors (Table 2) were identified and compared.

Table 1: Current pRIFLE criteria used for diagnosis of AKI[4]

pRIFLE	eCCl	UOP
R - Risk	eCCl>25%	<0.5 ml/kg/h for 8 h
I - Injury	eCCl>50%	<0.5 ml/kg/h for 16 h
F - Failure	eCCl>75% or	<0.3 ml/kg/h for 24 h
L - Loss	eCCl<35 ml/min/1.73 m^2	Or anuria for 12 h
E - End stage	Persistent failure>4 weeks	
	Persistent failure>3 months	

eCCl determined by the Schwartz formula: eCCl=CLCR = (k×Ht)/Serum Cr., where Ht height/length is in cm, serum creatinine in mg/dl and k is a constant (k=0.55 for all children except infants and k=0.45 for infants). GFR: Glomerular filtration rate, SCr: Serum creatinine concentration, eCCl: Estimated creatinine clearance, AKI: Acute kidney injury, pRIFLE: Pediatric Modified Risk, Injury, Failure, Loss, End-Stage Kidney Disease, UOP: Urine output

Table 2: Predictors of AKI using binary logistic regression analysis

Risk factors	No AKI *N*=64 (%)	AKI *N*=50 (%)	Multivariate *P* value	Adjusted OR	95% CI
Length of stay in PICU>4 days	38 (59.4)	41 (82)	0.163	2.112	0.73-6.035
PRISM≤10	32 (50)	38 (76)	0.142	2.036	0.788-5.25
Number days on mechanical ventilation≥4 days	14 (21.9)	25 (50)	0.244	1.806	0.66-4.89
Use of diuretics	57 (89.1)	37 (74)	0.047**	0.324	0.107-0.85
Nor-adrenalin used	28 (43.8)	28 (43.8)	0.718	1.171	0.49-2.74
OR: Odds ratio=OR=ad/bc					
OR<1: Negatively related					
OR=1: Not related					
OR>1: positively related					

PRISM: Pediatric risk of mortality, MODS: Multiorgan dysfunction syndrome

Statistical Methods

Descriptive statistical analysis has been performed in this study. Results on continuous measurements are presented on mean ± standard deviation (SD) (Min-Max), and those on categorical measurements are presented in *N* (%). Significance is assessed at 5% level of significance. Chi-square/Fisher exact test has been used to find the significance of study parameters on categorical scale between two groups.[12-15]

RESULTS

Out of 127 patients, 114 enrolled in the prospective pRIFLE validation study had urine specimens and SCr available for analysis. Five patients were excluded because they had less than two SCr levels drawn and eight patients had no urine sample available. Out of total 114 patients, 50 developed AKI and 64 patients (56.2%) did not develop AKI during the study period and served as controls; 23 patients (20.1%) developed pRIFLEmax R AKI; 15 (13.1%) pRIFLEmax I and 12 (10.5%) pRIFLEmax F AKI (Table 3).

Patients were classified into two groups, i.e., AKI and no AKI and baseline characteristics in both the groups were compared.

There were 35 male patients in AKI and 41 in non AKI group. The mean ± SD age of entire cohort was 4.2 ± 4.8 years range (1 month-16 years). Mean age of children in AKI group was 3.2 ± 3.6, whereas mean age in Non AKI group was 4.96 ± 5.02.

The mean ± SD weight of entire cohort was 16 ± 17.8 years range (10-36 kg). Mean weight of children in AKI group was 11.2 ± 12.6, whereas mean weight in non AKI group was 17 ± 18.02.

Risk Factors for AKI

Univariate analysis was performed to identify risk factors for AKI (Table 4). Out of 16 only three risk factors, i.e., duration of PICU stay, higher PRISM score and prolonged ventilator support were strongly significant ($P < 0.01$), and two suspected risks factors, i.e., use of nor adrenaline and diuretics were moderately significant ($P = 0.01 < P < 0.05$) (Figure 1).

Table 3: Incidence of AKI according to modified pRIFLE criteria

Classification	pRIFLE (UOP+Creat) *N*=114 (%)
No AKI	64 (56.2)
AKI	50 (43.8)
Risk	23 (20.1)
Injury	15 (13.1)
Failure	12 (10.5)

AKI: Acute kidney injury, pRIFLE: Pediatric Modified Risk, Injury, Failure, Loss, End-Stage Kidney Disease, UOP: Urine output

Subsequently multivariate logistic regression analysis (Table 2) was performed to identify independent risk factor for AKI which showed following results: Duration of PICU stay >4 days (82% vs. 59.4%, $P = 0.163$, odds ratio [OR] of 2.112, and 95% confidence interval [CI] [0.73-6.035]), PRISM >10 (76% vs. 50%, $P = 0.142$, OR of 2.036, 95% CI: 0.788-5.25), prolonged ventilation (50% vs. 21.9%, $P = 0.244$, OR of 1.806, 95% CI: 0.66-4.89) and use of nor adrenalin (28% vs. 28%, $P = 0.718$, OR of 1.171, 95% CI: 0.49-2.74) were found to have no relation with AKI whereas use of diuretics had negative correlation with AKI (89.1% vs. 74%, $P = 0.047$, OR of 0.324, 95% CI: 0.107-0.85) hence protective role in AKI.

DISCUSSION

Our single-center study evaluates the role of various factors in the development of AKI in PICU. This study shows that the incidence of AKI in PICU is 43.3% which is comparable with the other studies. Cerda J *et al.* reported that AKI affects approximately 35% of intensive care patients and 4-7% of all hospitalized patients.[5]

Table 4: Risk factors of AKI by univariate analysis

Risk factors	AKI *N*=50 (%)	No AKI *N*=64 (%)	*P* value
Age ≤1 years	40.0	21.9	0.124
Male	70	64.1	0.505
Weight<10 kg	26.6	26.6	0.128
Length of stay in PICU>4 days	82.0	59.4	0.009**
Pre-existing illness	24.0	18.8	0.495
PRISM III score>10	76.0	50.0	0.005**
Need for mechanical ventilation	72.0	73.4	0.864
≥4 days of ventilation	50.0	21.9	0.002**
Nor-adrenalin used	56	43.8	0.036*
Liposomal amphotericin used	12.0	3.1	0.136
Antiviral used (acyclovir)	46.0	29.7	0.073+
Use of diuretics	74.0	89.1	0.036*
Use of IV radiocontrast	68.0	65.6	0.790
Blood products used	46.0	42.2	0.684
Infections	34.4	28.0	0.467
MODS	1.6	8.0	0.167

IV: Intravenous, Significant figures: +Suggestive significance (*P*: 0.05<*P* < 0.10), *Moderately significant (*P*: 0.01<*P* < 0.05), **Strongly significant (*P*<0.01). MODS: Multiorgan dysfunction syndrome, PICU: Pediatric intensive care unit, PRISM: Pediatric risk of mortality score, AKI: Acute kidney injury

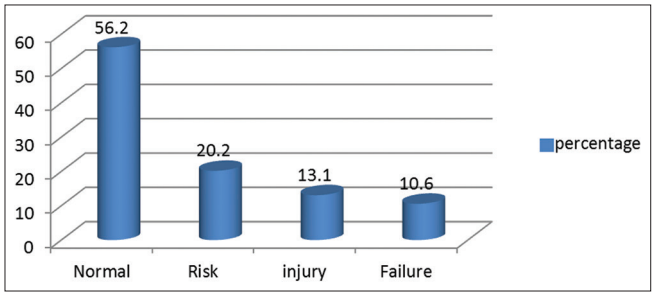

Figure 1: Incidence of acute kidney injury Pediatric Modified Risk, Injury, Failure, Loss, End-Stage Kidney Disease (urine output + creatinine)

The high prevalence of AKI on admission to PICU in our sample 50 out of 114 (42%) suggests that study of risk factors (clinical and biochemical) for developing AKI, may need to include data from patients before ICU admission.

On comparison of AKI and no AKI group, the age, weight, and gender were almost similar and found statistically insignificant ($P > 0.05$). The duration of PICU stay (>4 days), PRISM score >10, and prolonged need for mechanical ventilation >4 days was strongly significant ($P > 0.01$), use of nor-adrenalin, liposomal amphotericin, diuretics were moderately significant risk factors for AKI ($P < 0.05$).

However, binary logistic regression analysis showed that use of diuretics had a protective role (89.1% vs. 74%, $P = 0.047$, OR of 0.324, 95% CI: 0.107-0.85), whereas other factors had no role for the development of AKI in PICU however further studies need to be done to describe its role and benefit in critical patients.

Pre-existing illness, use of blood products, use of IV radiocontrast were also statistically insignificant risk factors ($P > 0.05$).

Potential limitations of our study include the relatively small sample size of 114; another potential concern is the use of an assumed baseline eCCl of 100 ml/min/1.73 m^2 for patients without a known baseline creatinine, in about one-fourth of the patients. The potential danger of this assumption would be to misdiagnose a patient with AKI based on a relative decrease in eCCl if, in fact, the patient had chronic kidney disease. Whether or not such misdiagnosis would lead to unnecessary evaluation or treatment is currently not known, but clinicians should exercise caution when classifying patients with AKI using pRIFLE, or any system using eCCl change when a baseline creatinine level is unknown.[9-15]

CONCLUSION

We conclude that multidimensional AKI classification and stratification systems, such as pRIFLE, can serve well to improve understanding of AKI epidemiology and potentially optimize evaluation and treatment for AKI in children.

Furthermore, as SCr and UOP seem to be late markers of renal injury, use of classification systems will be essential to assess the potential utility of urine and other serum biomarkers to detect AKI earlier, identify risk factors, and direct therapies to prevent or mitigate AKI in children before a rise in SCr concentration.

The global knowledge of the factors involved in the onset and prognoses of AKI is of fundamental importance regarding the management of critically ill patients hence this study found to be useful in predicting and managing AKI early and prevent the subsequent morbidity and mortality due to AKI and its complications.

We also suggest that use of diuretics in critically ill children is a protective factor of AKI, however, further studies need to be done to describe its role and benefit in critical patients.

Information on the overall incidence of AKI based on pRIFLE classification system, risk factors for AKI and the influence of AKI on outcome which occurs later for e.g., ESRD in pediatric patients may be useful in the design of larger multicenter trials to determine the contribution of AKI to patients' long-term morbidity and mortality which is not done in our study and to evaluate the effect of early initiation of aggressive measures to prevent and treat AKI in pediatric ICU patients.

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Original Article

Fetal Magnetic Resonance Imaging: A Problem Solving Tool in Antenatally Detected Fetal Anomalies and Abnormalities

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Abstract

Background: A study was conducted to confirm findings of antenatal ultrasonography (US) by magnetic resonance imaging (MRI) and to understand the role of fetal MRI in decision making for better parental counseling in case of central nervous system (CNS) anomalies.

Methods: The study was conducted in Department of Radiology, Manipal Hospital, over 24 months including all pregnant women with suspected fetal CNS anomalies on the US.

Results: A total of 29 patients underwent fetal MRI examination on GE 1.5 Tesla TWIN SPEED, HDX machine. 2/29 cases were twin pregnancies. In 1/2 twin pregnancy feto-reduction of a fetus was done. In 26/31 fetuses, comparison of US and MRI reports was made. MRI provided supplementary information to US in 35% (9/26) and it was concordant with US in 46% (12/26) while discordance observed in 19% (5/26). In 23% (6/26) US provided additional information over MRI.Ventriculomegaly was noted in 12/30 live fetuses (40%), in 2/12 (17%) it was severe, and in 6/12 (50%) associated CNS anomalies were found. In 6/29 fetuses (21%) corpus callosal abnormality was suspected on the US. In 5/6 (83%) MRI confirmed while in rest, it disproved US diagnosis. 5/30 (17%) fetuses had posterior fossa malformations. 1/30 had schizencephaly. 1/30 had tuberous sclerosis and single fetus showed unilateral deep asymmetric calcarine sulcus.

Conclusions: MRI allows detailed visualization of the fetal CNS. Additional findings provided by MRI are helpful in understanding severity of the abnormality and in decision making. The US is useful for initial screening and follow-up.

Key words: Fetal MRI, Central Nervous System anomalies, US correlatrion

INTRODUCTION

Ultrasonography (US) is the primary screening modality for fetal imaging because of its relatively low cost, lack of harmful effects, easy availability, and real-time imaging. However, there are limitations, including small field of view, limited soft tissue acoustic contrast, beam attenuation by adipose tissue, poor image quality in oligohydramnios and limited visualization of posterior fossa in advanced gestational age, because of calvarial calcification.[1-3]

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Magnetic resonance imaging (MRI) is a valuable complement to the US when additional information is needed to confirm diagnosis during pregnancy. Recently, MRI with fast sequences has allowed images to be obtained during maternal breath-holding, without fetal or maternal sedation. It gives superior soft tissue contrast resolution, because of which we are able to distinguish individual fetal structures such as lung, liver, kidney, and bowel.[4] Moreover, it provides multiplanar imaging as well a large field of view, facilitating examination of fetuses with large or complex anomalies, and visualization of the lesions within the context of the entire fetal body.[5] It allows better fetal imaging in situations such as maternal obesity and oligohydramnios, where it may be difficult to obtain clear images by the US due to technical limitations.[6]

MRI has also proved to be useful for a wide variety of disorders, mainly those involving the central nervous

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system (CNS); especially in late gestation when the ossification of the calvarium limits a good visualization of the encephalic structures. However, fetal MRI study may give limited diagnostic information in early gestational age due to the small size of the fetus and fetal movement.[7] Safety is important in evaluating the fetus. MRI is a non-invasive that does not involve ionizing radiation with no known associated side effects or reported delayed sequels.[8] No known harmful effects to the developing human fetus have been documented at 1.5 Tesla or less. However, safety has not been dogmatically proven. *In-utero* MRI has not shown any effect on fetal growth.[9] A 2 years follow-up study of children who underwent imaging *in-utero* showed no demonstrable increase in disease occurrence.[10]

The American College of Radiology (ACR) states that fetal MRI can be done at any stage of pregnancy if the risk-benefit ratio to the patient warrants the same[11] and only if the US is inadequate. However, it is wise to wait until 17-18 weeks of gestation because of the potential risk to the developing fetus and excessive motion of younger foetuses.[12] A written informed consent is usually required from the pregnant woman before fetal MRI.

METHODS

The study was conducted in the department of radiodiagnosis and imaging Manipal hospital Bengaluru, a 800 bedded multispecialty tertiary care hospital, over a period of 24-month from July 2012 to July 2014. All pregnant women with suspected fetal anomaly on ultrasound scan and above 18 years of age; pregnant women with previous history of fetal congenital anomalies; and pregnant women with confirmed diagnosis of congenital anomalies of fetus *in-utero* who are <18 weeks and are scheduled for termination were included in the study. Pregnant women having a history of claustrophobia, metallic implants insertion, cardiac pacemakers, and metallic foreign body were excluded from the study. MRI was also avoided in pregnant women who require sedation. A total of 29 patients underwent fetal MRI examination in our hospital during the study period.

GE 1.5 Tesla TWIN SPEED, HDX MRI machine was used. The non-imaging data were collected in prescribed format. 12 channel body coil was used with small field of view as possible. 3-5 mm thick slices were taken. Multiple sequences were taken predominantly T2 single shot fast spin echo (SSFSE) in 3 orthogonal planes. The mother was kept NPO for 4 h prior to the MRI exam to reduce fetal motion. Written informed consents were obtained before study in all cases. The mother lied supine during the course of the exam in comfortable position possible during the MR exam to minimize fetal motion. MRI exam can be performed with the mother lying on her left side although this results in lower image quality.

Most fetal MRI is primarily performed using an initial localizer obtained in 3 orthogonal planes with respect to the mother, using 6-8 mm thick slices with a 1-2 mm gap and a large field of view. The localizer is used to visualize the position of the fetus and determine fetal sidedness, as well as to ensure that the coil is centered over the region of interest. Typically, 3 mm thick ultrafast T2 weighted (T2W) images of the fetal brain were then prescribed from the localizer with no skip. Images were acquired in the axial, sagittal, and coronal planes.

Diffusion-weighted imaging was also used to identify focal areas of injury as well as to assess brain development using A B value of 0 s/mm^2 and 600 s/mm^2. The data were collected on pre-designed study performa. All the data were entered in Microsoft Excel Program and checked for any inconsistencies. Data were presented in terms of percentages and proportions.

RESULTS

About 29 patients underwent MRI in our department for different indications all of who were referred after the US. In 26/29 cases, MRI was done within 15 days of US. Age of the patients included in this study ranged between 19 and 34 years with an average age of 28 years. All MRI examinations were done in the second and third trimester. MRI examination was avoided in the first trimester in accordance to ACR guidelines to avoid potential risk to the developing fetus. All pregnant women included in this study were of 19-36 weeks of gestation with average gestational age of 26 weeks.

History of previous pregnancy with congenital anomalies was elicited in 5 patients. In our study, we have studied fetal anomalies involving CNS. In 4/5 patients CNS abnormality was found in present pregnancy.

In 4/29 patients, detailed US report was not available. In 2/29 cases were twin pregnancies. In one twin pregnancy, laser ablation of umbilical artery of one fetus was done for twin-twin transfusion syndrome. Thus, in 26/31 fetuses comparison between US and MRI reports was made.

As shown in Figure 1 in 12/26 fetuses (46%), the diagnoses established by the US were confirmed by MRI. MRI imaging provided more information than did the US in 9/26 fetuses (35%). There were 6/26 fetuses in which US provided additional information to that provided with

MRI in terms of intrauterine growth restriction (IUGR), Rhabdomyomas in the case of tuberous sclerosis, cleft lip, cleft palate, and limb anomalies. Discrepancies occurred in 5/26 fetuses (19%) details of which are given in Table 1.

The criterion used in our study to measure ventricles was same as for ultrasound. It was considered mild when it measured 10-15 mm, moderate when >15 mm with >3 mm of adjacent cortical thickness and severe when ventriculomegaly with <2 mm of adjacent cortical thickness. In our study, we found ventriculomegaly in 12/30 (40%) fetuses. 8/12 cases (66%) were bilateral, and rests were unilateral. 2/12 cases (17%) of ventriculomegaly were of severe category. 3/12 (25%) were of moderate category while 7/12 (58%) cases had mild ventriculomegaly (Figure 2). In 6/12 cases (50%), we have found various associated CNS anomalies which included sulcation abnormality, agenesis of corpus callosum, and germinal matrix bleed.

In 3/7 (43%) cases of mild ventriculomegaly, associated anomalies were detected. In 3/7 (43%) patients pregnancy was terminated, 2 of which did not have associated anomaly. 1/7 case was lost follow-up, which had associated partial agenesis of corpus callosum. 2/4 cases of mild ventriculomegaly and no associated anomaly continued pregnancy, one of which had normal delivery with normal postnatal neurosonogram while another pregnancy was ongoing. 2/4 cases of mild ventriculomegaly and no associated anomaly underwent termination of pregnancy despite isolated nature of ventriculomegaly. 2/7 cases (29%) delivered with normal early milestones.

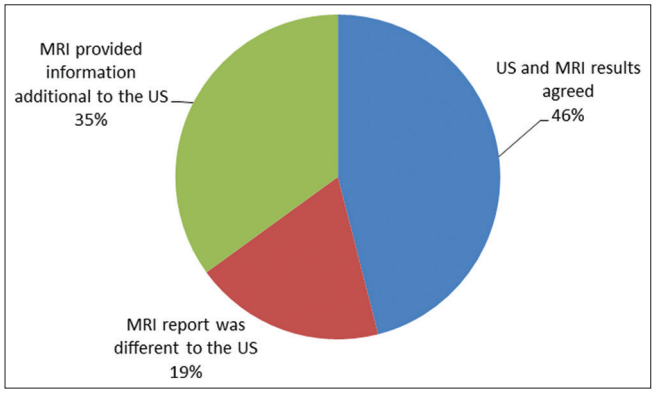

Figure 1: Comparison between ultrasonography and magnetic resonance imaging findings

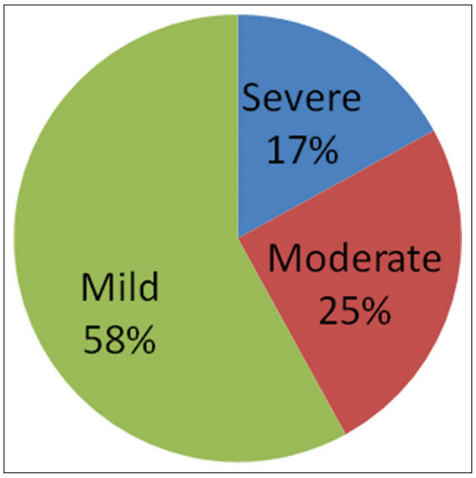

Figure 2: Ventriculomegaly

In 6/29 (21%) corpus callosum was not visualized on the US or had suspected corpus callosal abnormality. In 5/6 cases (83%) MRI confirmed US findings. In 1/6 cases MRI disproved US diagnosis of agenesis of corpus callosum. 1/6 cases were lost follow-up. In 1/6 cases pregnancy was terminated. In 4/6 cases child had normal early milestone although postnatal imaging was not available.

Sulcation pattern was normal for age in 29/30 fetuses. In single fetus, it showed time lag of 2-3 weeks.

5/30 had posterior fossa malformations. 2/5 were of Dandy-Walker continuum, one case was of isolated inferior vermian hypoplasia, one of unproven partial rhombencephalosynopsis, and one of arachnoid cyst.

1/30 fetuses had schizencephaly which appears as grey matter lined cleft extending from ependyma to pia matter; (Figure 3). 1/30 fetuses had tuberous sclerosis. In 1/30 case unilateral deep asymmetric calcarine sulcus (CS) was found.

2/29 cases lost follow-up. Follow-up was available in 27/29 patients. 2/29 cases were twin pregnancies. In 1/2 twin pregnancy feto-reduction by laser ablation of umbilical artery was done, emergency lower section caesarean section was done, and surviving fetus was normal. Another twin pregnancy was terminated. In 14/25 cases pregnancy was continued. In 11/25 cases patient underwent termination or pregnancy terminated spontaneously or pregnancy had terminated due to the maternal indication.

DISCUSSION

Due to increased social awareness and improved antenatal care facilities, there is active participation from the community in the field of antenatal care. Thus, the number of antenatal US scans has increased significantly in recent time, which is partly responsible for increased anomaly detection rate; thus, making the development possible in the field of US and MR technology.

Major indications for fetal MRI were confirmation of inconclusive sonographic findings and the evaluation of sonographically occult diagnoses.

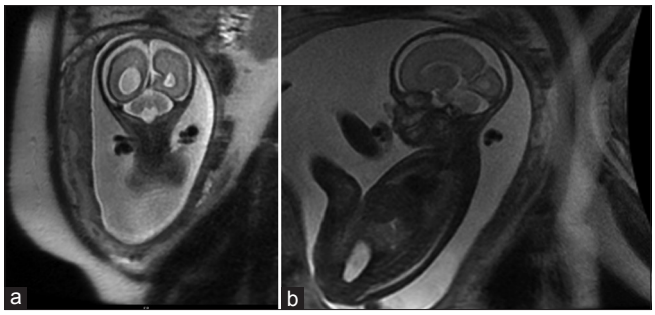

Figure 3: (a and b) T2 weighted sagittal, and coronal images of 27W fetus showing Fluid filled tract on the medial aspect of the right parieto-occipital lobe (arrow) with no connection to the ventricles suggestive of right deep calcarine sulcus

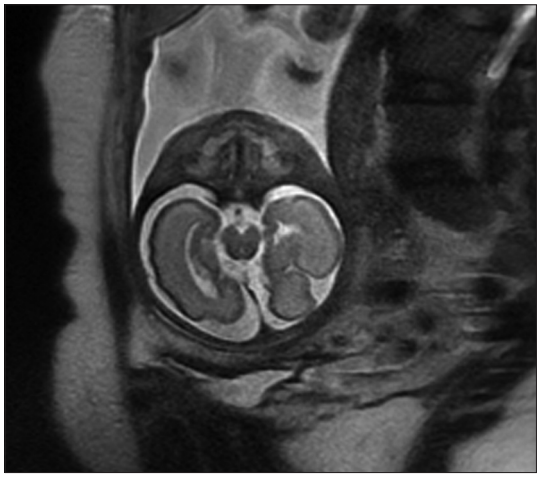

Figure 4: T2 weighted images of 23W fetus with gray matter lined tract (arrow) in the left parietotemporal region communicating with left lateral ventricle with associated dimpling of the left lateral ventricle suggestive of schizencephaly

History of previous pregnancy with congenital anomalies is a risk factor for congenital anomaly. In pregnancies with a history of congenital abnormalities, anomalies were found in present pregnancy in 4/5 (80%) (Table 2).

Whitby *et al.,* 2003,[15] did a prospective, observational study of 21 pregnant women of 19-36 weeks of gestation whose fetuses were thought to have a CNS abnormality on the basis of antenatal US. They found that MRI report was different to the US in 10/21 (47.6%); MRI provided information additional to the US in 5/21 (23.8%) and US and MRI results agreed in 6/21 (28.6%).

In study conducted in our institute, MRI report was different to the US in 19%, MRI provided information additional to the US in 35%, US and MRI results agreed in 46%. There were 23% fetuses in which US provided additional information to that provided with MRI in terms of IUGR, rhabdomyomas in the case of tuberous sclerosis, cleft lip, cleft palate, limb anomalies, vertebral anomalies (Table 2).

In our study 46% cases, diagnoses established by the US were confirmed by MRI compared to their study in which it was 28.6%. Indicating that diagnosis of congenital anomalies with the US has been improved reaching up to 46% in our study. This can be explained by the advances in US technology like 3D, 4D, software like Omni view, tomographic ultrasound imaging, and the radiologist's operative and interpretation skills particularly in last decade.

The conventional ultrasound is still the standard in diagnostic ultrasound studies. In the new 3D fetal scanning technology, sound waves are sent at different angles and returning echoes are processed by sophisticated software resulting in a reconstructed three-dimensional (3D) volume image of fetus's surface or internal organs. 3D ultrasounds allow one to see width, height and depth of images but no movement is shown. The latest 4D fetal ultrasounds are similar to 3D scans, with the difference associated with time. 4D allows a 3D picture in real time, rather than delayed, due to the lag associated with the computer constructed image, as in classic 3D ultrasound. The volume data acquisition also allows us to interpret images in various sectional planes where we can manipulate slice thickness. This is useful in objective assessment of the brain surface, to detect the cranial bone abnormality as well as in migration disorders and cortical development.

Fetal echocardiography has experienced vast development along with high resolution, and real-time scanning. Doppler flow examinations have improved detection rate of the fetal cardiac anomalies. Hence, even detection of intraventricular rhabdomyomas of heart was possible as in our case US had limitations in cases of maternal obesity, improper fetal position, Oligohydramnios, improper visualization of the fetal structures in cases of post acoustic shadowing due to bony structures, where MRI plays a significant role in decision making.

In 35% cases, MRI gave additional information in our study which was 23.8% in study done by Whitby *et al.* indicating improved MRI diagnosis also.

Excellent tissue contrast, large field of view, superior soft-tissue contrast resolution, and the ability to distinguish individual structures are the advantages of MRI. Development of fast T2W sequences like steady state free precession sequence (SSFSE) has made available the assessment of the intracranial structure. The examination time is reduced significantly reaching to minimum of 10-15 min in our institute. Overall, the benefits of fetal MRI are much more in CNS anomalies than in non-CNS anomalies.

Diffusion MRI is very helpful for early detection of fetal hypoxia. MR Spectroscopy is potential new advances in MRI whose role needs to be explored.

Table 1: Findings in present pregnancy in patients having history of previous pregnancy with congenital anomalies

History of pregnancy with congenital abnormalities	Present pregnancy
Joubert's syndrome	Normal
CDH, ventriculomegaly, micrognathia, microcephaly	Bilateral mild ventriculomegaly. Multiple foci of T2 hypointensity around lateral ventricles. DD-old hemorrhage or small tubers. Poorly visualized posterior corpus callosum
ACC; unilateral ventriculomegaly	Bilateral mild ventriculomegaly. Partial ACC
Microcephaly ACC	Good visualization of corpus callosum anteriorly, poorly visualized posteriorly-probably just forming. Suggested follow-up
Ventricular septal defect	Left choroid plexus cyst

ACC: Agenesis of corpus callosum, CDH: Congenital diaphragmatic hernia

Table 2: Details of cases where discrepancies between US and MRI was observed

US findings	MRI findings
Asymmetric IUGR. Bilateral mild ventriculomegaly? Dueto lissencephaly. Corpus callosum is normal	Bilateral mild ventriculomegaly. No other abnormality
Lateral ventricle appeared pinched out and lifted up, measurement could not be taken	Schizencephaly in the left parietotemporal region. No other abnormality
Three cysts in the right cerebral hemisphere (arachnoid cysts) displacing falx to left and not communicating with the meningeal spaces. Bilateral ventriculomegaly (right - 16.4 mm; left-11 mm)	Interhemispheric cyst with few thin septae. Bilateral moderate ventriculomegaly
CSP was not visualized. Pericallosal artery not seen suggestive of ACC. Bilateral Mild to moderate ventriculomegaly	Bilateral Mild to moderate ventriculomegaly. NoACC
Bilateral ventriculomegaly	Unilateral moderate ventriculomegaly

ACC: Agenesis of corpus callosum, CSP: Cavum septum pellucidum, US: Ultrasonography, MRI: Magnetic resonance imaging, IUGR: Intrauterine growth restriction

Discrepancies occurred in 5/26 (19%) cases which were 47.6% in their study, significantly reducing incorrect interpretation rates. This again can be explained by improvements in ultrasound equipment and skills along with advances in MRI and their interpretation.

The impact of fetal MRI on treatment can be particularly difficult to assess because a contemporaneous standard of reference was lacking in our setting. Furthermore, studies in which fetal MRI performed at academic centers is compared with sonography performed at other hospitals or diagnostic centers, rather than sonography performed at equivalent academic centers, which tend to exaggerate the apparent advantages of MRI.

In a study done by Frates *et al*., 2004[4] images of 27 fetuses (28 diagnostic cases) with anomalies diagnosed at US were evaluated. Prenatal US and MRI imaging findings were compared with postnatal diagnoses which were an added advantage, compared to our study. In 7/28 (25%) diagnostic cases, US and MRI imaging findings were in complete agreement with postnatal diagnoses. MRI imaging correctly provided additional information to the US determined diagnosis in another 7/28 (25%) and correctly changed the US diagnosis in 3/28 (11%). The MRI imaging-determined diagnosis was incorrect, and the US diagnosis was correct in 4/28 (14%). In 7/28 (25%) cases, the diagnoses at both US and MRI imaging were incorrect when correlated with the postnatal outcome.

In comparison to our study where in US and MRI results agreed in 46%, they found it to be 25%. MRI imaging correctly provided additional information to the US-determined diagnosis in another 25% in their study which was found to be 35% in our study. This discrepancy can be explained by the fact that they have not included the cases where US and MRI imaging were incorrect when correlated with the postnatal outcome. In our study, postnatal diagnosis like autopsy or imaging was unavailable as most patients were not willing for the same after termination.

Hosny *et al*., in 2010[16] examined 25 pregnant women with MRI in whom US detected fetal congenital anomalies. MRI findings altered the diagnosis of 2/25 (8%) cases. MRI added additional findings two out of 4 cases. In the remaining 18/25 (72%) cases MRI confirmed the diagnosis of US. Compared to this study where US and MRI were in agreement in up to 72% case, in our study it was found it to be 46%. As in our study, they also did not include postnatal follow-up like autopsy or imaging.

In one interesting case, unilateral deep asymmetric CS was found which is normal developmental variant as shown in Fig.4. It is most commonly found on the right side as in our case. This can be mistaken as schizencephaly, thus careful evaluation should be made to differentiate both entities (Figure 3).

Evaluation of corpus callosum is much better with MRI where it is directly visualized unlike US which relies on indirect signs. In 21% corpus callosum was not visualized on US or had suspected corpus callosal abnormality. In 83% MRI confirmed US findings. In 1/6 cases MRI disproved US diagnosis of agenesis of corpus callosum.1/6 cases was lost follow-up. In 1/6 cases pregnancy was terminated. In 4/6 cases child had normal early milestone although postnatal imaging was not available. This proves deductions made by Glenn *et al.,* 2005[17] in their study about the upper hand of MRI in evaluation of corpus callosum.

In 3/7 (43%) cases of mild ventriculomegaly, associated anomalies were detected. In 3/7 (43%) patients pregnancy was terminated, 2 of which did not have associated anomaly. 1/7 case was lost follow-up, which had associated partial agenesis of corpus callosum. 2/4 cases of mild ventriculomegaly without associated anomaly continued pregnancy, one of which had normal delivery with normal postnatal neurosonogram while another pregnancy was ongoing. 2/7 cases (29%) delivered with normal early milestones. 2/4 cases of mild ventriculomegaly and no associated anomaly underwent termination of pregnancy despite isolated nature of ventriculomegaly.[13,14]

Reported fetal anomaly on ultrasound can add to mother's metal stress in Indian scenario. Having pregnancy with fetal anomaly adds social burden to parents forcing them to think in favor of termination of pregnancy. Thus, apart from the general need for psychological support to women undergoing prenatal examinations, there may be a need for additional support. Prenatal counseling helps the family to decide between prenatal or postnatal therapies or the termination of the pregnancy. Prenatal MRI can help in management decisions in such cases.

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Original Article

Association of Lipid Profile, Body Mass Index, and Waist Circumference as Cardiovascular Risk Factors for Obese Male Adults of North India

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Abstract

Background: Obesity is one of the most important modifiable risk factors in the pathogenesis of cardiovascular disorders such as atherosclerosis hypertension and type-2 diabetes mellitus. The aim of the study was to evaluate the association of obesity, plasma lipid profile, and atherogenic indices as markers for cardiovascular diseases (CVD) among North Indian population.

Method: A cross-sectional study in a randomly selected sample was conducted in 70 subjects 18-58 years of age. Anthropometric measurements, including body weight, height, waist circumference (WC), and body mass index (BMI) were calculated. The subjects were divided into 4 groups in two categories. Group A (BMI< 25 kg/m^2) and Group B (BMI >25 kg/m^2), Group C (WC< 90 cm) and Group D (WC >90 cm). Total cholesterol (TC), high-density lipoprotein-cholesterol (HDL-C), Low-density lipoprotein-cholesterol (LDL-C), and triglycerides (TG) were measured, and atherogenic index (AI) was calculated.

Results: Group B had significantly higher BMI when compared with Group A (P <0.0001). Group B had a nonsignificantly increased risk of high TC (P = 0.27), TG (P = 0.08) and significant increased risk of high (LDL) (P <0.01), AI (P <0.001), and low HDL-C (P < 0.001) compared with Group A. Group D had significantly higher WC when compared with Group C (P < 0.0001). Group D had a nonsignificantly increased risk of high TC (P = 0.86), LDL-C (P = 0.41) and significantly increased TG (P < 0.05), AI (P < 0.05), and low HDL-C (P < 0.01). The partial correlation coefficient for the cardiovascular risk marker of BMI indicated a positive significant association with TC (R = 0.345, P =0.003), TG (R = 0.223, P = 0.06) and LDL-C (R = 0.342, P = 0.003), AI (R = 0.46, P <0.001), and negative with HDL-C (R = -0.381, P = 0.001). For WC indicated a positive significant association with TC (R = 0.205, P = 0.096), TG (R = 0.283, P = 0.018), and LDL-C (R = 0.16, P = 0.185), AI (R = 0.29, P = 0.014), and negative with HDL-C (R = −0.301, P = 0.011). Obesity significantly increased the risk of atherosclerosis (assessed by AI).

Conclusion: Obese people screened by the World Health Organization reference values are at increased risk of CVD in adults.

Key words: Body mass index, Cardiovascular risks, Lipid profile, Obesity, Waist circumference

INTRODUCTION

Cardiovascular diseases (CVD); the leading cause of morbidity and mortality in the western world, are now emerging public health challenges in developing countries,[1] accounting for 80% of deaths and 87% of related disability currently recorded in the low-and middle-income countries.

In India, CVD accounts for 31.7% of total deaths. In developing countries, mortality due to CVD is expected to rise to 19 million by 2020.[2]

In the Indian subcontinent, CVD manifests itself almost 10 years earlier on an average compared with the rest of the world, in western countries, CVD accounts for only 23% of the CVD deaths occurring below the age of 70

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compared to 52% of CVD deaths below the age of 70 in India.[3] The association between dyslipidemia, obesity, and hypertension is well established and all have been found to be major risk factors for the development of CVD, a leading cause of visits to physicians and cause of death.[4-6]

Blood cholesterol has long been recognized as a major independent risk factor for CVD in adults. More recently, the level of triglycerides (TG) has been incriminated as a CVD risk factor independent of cholesterol.[7]

However, obese individuals differ not only in the amount of excess fat that they store but also in the regional distribution of the fat within the body. In adults, intra-abdominal adipose tissue is the most clinically relevant type of body fat, apart from total body fat.

Some studies have shown that waist circumference (WC) may be a better predictor of CVD than body mass index (BMI) and waist-hip ratio.[8] A population is viewed as much vulnerable to dyslipidemia and other cardiovascular risk factors due to the western lifestyle, such as alcohol consumption, cigarette smoking, sedentary life, and consumption of diet with high fat contents, all of which are associated with abnormal lipid metabolism. Therefore, this study was designed to investigate the association of obesity, plasma lipid profile, and atherogenic indices as markers for CVD among North Indian population.

MATERIALS AND METHODS

This study was conducted on a total of 70 men (aged 18-58 years), including both the students of M B B S and Faculty Members in the Shri Guru Ram Rai Institute of Medical and Health Sciences, Dehradun for lipid profile. The subjects were briefed about the study, and their consent was taken.

Subjects with the history of diabetes mellitus, hypertension, coronary heart disease, and endocrinopathy or subjects taking any lipid-altering medicine were excluded from the study.

Anthropometric measurements such as height, weight and WC of each subject were recorded, and BMI was calculated. A fasting venous blood sample was drawn from each subject for lipid profile.

The subjects were divided into 4 groups in two categories based on BMI and WC cut-off points.

Groups Based on BMI Cut off Points

- Group A, it consists of 37 with their BMI <25 kg/m^2
- Group B, it consists of 33 subjects with their BMI >25 kg/m^2

Groups Based on WC Cut off Points

- Group C, it consists of 51 subjects with their WC <90 cm
- Group D, it consists of 19 subjects with their WC >90 cm

This study was conducted with the aim of comparing lipid profile and atherogenic index (AI) in normal weight, and obese subjects according to their BMIs and WC as markers for CVD.

Anthropometric Measurements

Weight

It was measured in kilograms (kg) to the nearest 0.5 kg on a portable weighing scale with the subject in light clothing and without shoes.

Height

It was measured in centimeters (cm) to the nearest 0.1 cm with the subject standing against the vertical wall with no shoes, heels together and heels buttocks, shoulders, and head touching the vertical wall surface.

BMI

It was calculated using the formula:

Weight (kg)/Height (m^2).

WC

It was measured in centimeters (cm) to the nearest 0.1 cm, at the level of umbilicus, at the end of expiration with person breathing silently, and using a flexible plastic tape.

Biochemical Parameters

A morning venous blood sample after an overnight fast (10-12 h) was drawn at each clinic unit. The blood samples were placed on ice until separation within 2 h. The samples were centrifuged at 2000 g for 5 min, after which plasma was isolated into dry plain plastic screw-capped containers and stored frozen −20°C before analyses. Plasma total cholesterol (TC) and TG concentrations were determined by enzymatic colorimetric assay as described above and modified by Richmond, and high-density lipoprotein-cholesterol (HDL-C), and low-density lipoprotein-cholesterol (LDL-C) were determined enzymatically after precipitation of other lipoproteins as described by Burstein *et al.* and Assmann *et al.*, respectively, using kits from Biosystem laboratories.[9-12] All samples were analyzed in duplicates, after which the mean was determined. AI was calculated for individual subjects by the equation:

AI = [(TC - HDL-C)/HDL-C].[13]

Cut-off Values

The World Health Organization reference values were adopted for classification of obesity.[14] Abdominal obesity was defined as having a WC 90th percentile for age and gender.[15] The cutoff values from the national cholesterol education program lipid assessments were adopted.[16] Abnormalities in lipid levels have traditionally been defined as concentrations 95th percentile for TC, TG, and LDL-C, whereas low HDL-C concentrations have traditionally been defined as, 5th percentile. All samples were analyzed in duplicates, after which the mean was determined.

The normal values of lipid profile used in our study are:

- TC: <200 mg/dl
- TG: <150 mg/dl
- LDL: <130 mg/dl
- HDL: >40 mg/dl

Statistical Analysis

The significance between the standard errors of means of different sets of observation was assessed by applying student's - *t*-test and 95% level of confidence ($P < 0.05$). Pearson's correlation coefficient was calculated between the anthropometric measurements (BMI and WC) and lipid profile (TC, TG, LDL-C, AI, and HDL-C).

OBSERVATIONS AND RESULTS

The subjects included in this study were divided into 4 groups in two categories based on BMI and WC cut-off points.

Group A - age group 18-58 years (mean 31.05 + 10.63 years) with BMI< 25 kg/m^2 (mean 21.41 ± 1.87 kg/m^2), Group B - age group 18-58 years (mean 33.55 ± 12.96 years) with BMI> 25 kg/m^2 (mean 27.69 ± 1.97 kg/m^2), Group C - age group 18-58 years (mean 31.37 ± 11.5 years) with WC <90 cm (mean 80.23 ± 5.24 cm), and Group D - age group 19-58 years (mean 34.53 ± 13.30 years) with WC >90 cm (mean 96.44 ± 5.39 cm).

Comparison of Lipid Profile According to BMI

TC

In Group A, it ranged from 96 to 220 mg/dl with mean of 146.73 ± 33.96 mg/dl (mean±standard deviation [SD]). In Group B, it ranged from 120 to 216 mg/dl with mean of 155.30 ± 30.3 mg/dl (mean±SD). It was statistically not significantly increased in Group B when compared with Group A ($P > 0.05$, Table 1).

TG

In Group A, it ranged from 90 to 350 mg/dl with mean of 133.89 ± 50.56 mg/dl (mean±SD). In Group B, it ranged from 82 to 349 mg/dl with mean of 158.30 ± 63.26 mg/dl (mean±SD). It was statistically not significantly increased in Group B when compared with Group A ($P > 0.05$, Table 1).

Table 1: Parameters based on BMI

Variables	Nonobese (Group A) *n*=37	Obese (Group B) *n*=33	*P*
Age (years)	31.05±10.63	33.55±12.96	0.38
BMI (kg/m^2)	21.41±1.87	27.69±1.97	<0.0001*
TC (mg/dl)	146.73±33.96	155.30±30.37	0.27
TG (mg/dl)	133.89±50.56	158.30±63.26	0.08
LDL-C (mg/dl)	72.15±36.39	94.27±18.46	0.0019*
AI	2.17±1.07	3.11±0.721	0.0001
HDL-C (mg/dl)	47.76±8.35	41.33±5.63	0.00031*

BMI: Body mass index, TC: Total cholesterol, TG: Triglycerides, LDL-C: Low-density lipoprotein-cholesterol, AI: Atherogenic index, HDL-C: High-density lipoprotein-cholesterol. Data are presented as the mean±standard deviation. *P<0.05, statistically significant when compared with nonobese or obese

LDL-C

In Group A, it ranged from 13 to 158 mg/dl with mean of 72.15 ± 36.39 mg/dl (mean±SD). In Group B, it ranged from 43.4 to 121 mg/dl with mean of 94.27 ± 18.46 mg/dl (mean±SD). It was statistically highly significantly increased in Group B when compared with Group A ($P < 0.01$, Table 1).

HDL-C

In Group A, it ranged from 31 to 67 mg/dl with mean of 47.76 ± 8.35 mg/dl (mean±SD) In Group B, it ranged from 32 to 57 mg/dl with mean of 41.33 ± 5.63 mg/dl (mean±SD). It was statistically highly significantly decreased in Group B when compared with Group A ($P < 0.01$, Table 1).

AI

In Group A, it ranged from 0.81 to 5.18 mg/dl with mean of 2.17 ± 1.06 (mean±SD). In Group B, it ranged from 1.79 to 5.55 with mean of 3.11 ± 0.72 (mean±SD). It was statistically highly significant increased while compared Group A with Group B ($P < 0.01$) (Table 1).

Comparison of Lipid Profile According to WC

TC

In Group C, it ranged from 96 to 220 mg/dl with mean of 153.98 ± 31.73 mg/dl (mean±SD). In Group D, it ranged from 114 to 210 mg/dl with mean of 155.37 ± 29.54 mg/dl (mean±SD). It was increased in Group D while compared with Group C, but the difference was not statistically significant ($P > 0.05$, Table 2).

TG

In Group C, it ranged from 82 to 350 mg/dl with mean of 136.76 ± 54.94 mg/dl (mean±SD). In Group D, it ranged from 90 to 284 mg/dl with mean of 169.10 ± 60.23 mg/dl (mean±SD). It was increased in Group D while compared with Group C and the difference was statistically significant ($P < 0.05$, Table 2).

LDL-C

In Group C, it ranged from 13 to 158 mg/dl with mean of 80.14 ± 34.06 mg/dl (mean±SD). In Group D, it ranged from 43.4 to 120 mg/dl with mean of 85.93 ± 22.33 mg/dl (mean±SD). It was increased in Group D while compared with Group C but the difference was not statistically significant ($P > 0.05$, Table 2).

HDL-C

In Group C, it ranged from 31 to 67 mg/dl with mean of 46.39 ± 8.15 mg/dl (mean±SD). In Group D, it ranged from 32 to 48 mg/dl with mean of 40.26 ± 4.72 mg/dl (mean±SD). It was statistically highly significantly decreased in Group D while compared with Group C ($P < 0.01$, Table 2).

AI

In Group C, it ranged from 0.81 to 5.55 l with mean of 2.17 ± 1.06 (mean±SD). In Group D, it ranged from 0.81 to 4.52 l with mean of 3.11 ± 0.72 (mean±SD). It was statistically significantly increased in Group D while compared with Group C ($P < 0.05$, Table 2).

Correlation of BMI and WC with Lipid Profile

BMI was positively correlated with TC (R = 0.34), TG (R = 0.22) LDL-C (R = 0.34), and AI (R = 0.46). The correlation was found to be statistically highly significant with TC ($P < 0.01$). LDL-C ($P < 0.01$) AI ($P < 0.001$), and statistically nonsignificant with TG ($P > 0.05$) (Table 3).

BMI was negatively correlated with HDL-C (R = −0.39). The correlation was found to be statistically highly significant ($P < 0.01$) (Table 3).

Table 2: Parameters based on WC

Variables	Nonobese (Group C)	Obese (Group D)	*P*
Age (years)	31.37±11.15	34.53±13.30	0.32
WC (cm)	80.23±5.24	96.44±5.39	<0.0001*
TC (mg/dl)	153.98±31.73	155.37±29.54	0.86
TG (mg/dl)	136.76±54.94	169.10±60.23	0.039*
LDL-C (mg/dl)	80.14±34.06	85.93±22.33	0.41
AI	2.46±1.04	3.03±0.91	0.03*
HDL-C (mg/dl)	46.39±8.15	40.26±4.72	0.003*

TC: Total cholesterol, TG: Triglycerides, LDL-C: Low-density lipoprotein-cholesterol, AI: Atherogenic index, HDL-C: High-density lipoprotein-cholesterol, WC: Waist circumference. Data are presented as the mean±standard deviation. *P<0.05, statistically significant when compared with nonobese or obese

Table 3: Correlation coefficient analysis

Variables	TC	TG	LDL-C	HDL-C	AI
BMI	0.34**	0.22	0.34**	−0.38**	0.46***
WC	0.20	0.28*	0.16	v0.30**	0.29**

TC: Total cholesterol, TG: Triglycerides, LDL-C: Low-density lipoprotein-cholesterol, AI: Atherogenic index, HDL-C: High-density lipoprotein-cholesterol, WC: Waist circumference, BMI: Body mass index. *P < 0.05, **P < 0.01, ***P < 0 0.001

WC was positively correlated with TC (R = 0.20), TG (R = 0.28) LDL-C (R = 0.16), and AI (R = 0.29). The correlation was found to be statistically nonsignificant with TC ($P > 0.05$), LDL-C ($P > 0.05$) and statistically significant with TG ($P < 0.05$) and AI ($P < 0.05$), and WC was negatively correlated with HDL-C (R = −0.30). The correlation was found to be statistically significant ($P < 0.01$) (Table 3).

DISCUSSION

This study evaluated the relationship of lipid profile, BMI, and WC as cardiovascular risk factors with obesity in adults. The main findings of this study were that obese subjects had statistically significantly more adverse cardiovascular risk factors; increased BMI and WC, hypercholesterolemia, hypertriglyceridemia, and more AI, with lower levels of HDL-C as compared to nonobese subjects (Figures 1 and 2).

Several studies have shown that the association between obesity and cardiovascular risk begins early in life.[17] BMI and WC; each measure a distinct component of obesity or body fat distribution, and WC are consistently the best predictors of cardiovascular risk.[18] The results of this study showed significant positive correlations between BMI,

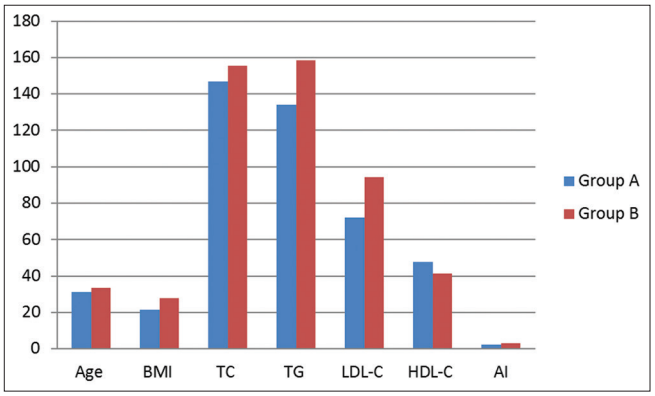

Figure 1: Variables in two groups based on body mass index

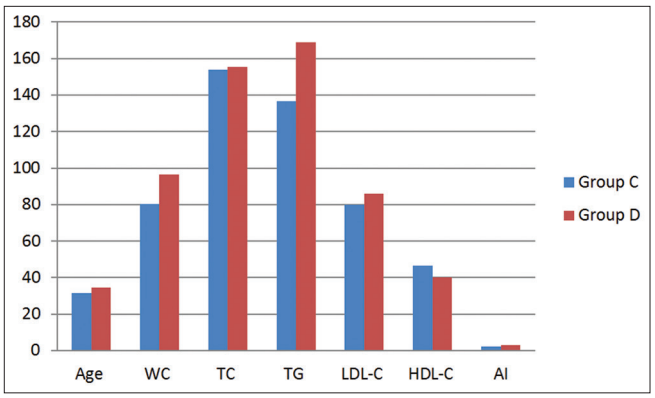

Figure 2: Variables in two groups based on waist circumference

WC and TC, TG, AI and nonsignificant with LDL-C, and an inverse correlation with HDL-C after adjustment for age. Abnormal serum lipid levels, especially decreased HDL-C and elevated TC, TG, LDL-C, and AI are generally recognized as independent risk factors for CVD.[19] Our study demonstrated an abnormal lipid profile with regard to elevated TC, TG, LDL-C, and AI, and reduced HDL-C in overweight or obese.

BMI and Lipid Profile

When compared according to BMI a nonstatistically significant increase in TC ($P > 0.05$) and TG ($P > 0.05$), and statistically significant increased LDL-C ($P< 0.01$), and statistically significant decreased HDL-C ($P < 0.001$) level in obese compared to nonobese but both the groups were having values within normal range. This finding was similar to observation reported by Regina Fisberg *et al.*,[20] While Njelekela *et al.* observed a significant increase in TC level in obese men.[21] Similar observations were made by Bertsias *et al.,* Mataix *et al.*, and Nagila *et al.* in their study.[22-24]

AI was found to be highly statistically significantly increased ($P < 0.001$) in obese compared to nonobese, which was also shown by studies of Rizk and Yousef,[25] Ugwuja *et al.* also observed an increased AI in obese subjects.[26]

WC and Lipid Profile

When compared according to WC obese subjects were found to have increased level of TC, TG, and LDL-C levels as compared to nonobese, but the difference observed was not statistically significant ($P > 0.05$) in TC and LDL-C levels but was significant in TG ($P < 0.05$) and AI (<0.05). A similar finding was reported by Mataix *et al.* who also observed no statistically significant difference in these lipid levels in obese and nonobese men.[23] Bertsias *et al.* found statistically significant increase in TC, TG and LDL-C levels, and decreased HDL-C ($P < 0.01$).[22] Ugwuja *et al.* also observed an increased AI in obese subjects.[26]

Correlation between Anthropometric Variables and Lipid Profile

Anthropometric variables viz. BMI and WC were correlated positively with TC, TG, LDL-C, and AI while correlated negatively with HDL-C. TC, TG, HDL-C, AI correlated significantly with BMI, and WC. LDL-C correlated statistically nonsignificantly with WC. Similar observations were also reported in the previous studies.[25-30] This may be attributed to the different age distribution of subjects as well as to the ethnic variations in fat distribution.

WC has been shown to be better predictors of dyslipidemia than BMI.[27] This study found BMI as a better predictor of dyslipidemia than WC (Table 3) which may be due to the younger population under study or due to ethnic variations in fat distribution. Kondo *et al.* also found the BMI as a better predictor of metabolic risk factors than WC.[31]

Thus, obesity measured by any of the anthropometric variable is an important contributor to dyslipidemia.

In summary, this study indicates that the combination of elevated TC, TG, AI and LDL-C, and decreased HDL-C, with BMI and, WC above the 90th percentile in obese, would place them at greater risk for CVD. These data are consistent with the previous studies in different ethnic groups.[32] Further studies are needed in larger sample sizes to investigate if other biomarkers could be used to define obesity and the implications for early detection of increased cardiovascular risk.

This study was limited by its small sample size. Blood pressure was not measured, which limits the associations of obesity with the metabolic syndrome as a cluster of potential risk factors for atherosclerotic CVD and type-2 diabetes.

CONCLUSION

Thus, it is concluded that the parameter indicating increased cardiovascular risk such as high TC, TG, LDL-C, AI, and low HDL-C in obese group as compared to nonobese. As TG, TC, LDL-C, and AI showed positive correlation while HDL-C showed a negative correlation with both BMI and WC. Hence, both the anthropometric indices (i.e., BMI and WC) can be used both alone and also in combination as a predictor of abnormal lipid profile and as a cardiovascular risk also.

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Original Article

Sexual Dimorphism of Digit Ratio (2D:4D) in Madhya Pradesh

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Abstract

Introduction: The ratio between the length of the 2nd and 4th digit (2D:4D) is sexually dimorphic, with mean male 2D:4D lower than mean female 2D:4D, which will prove useful to determine sex when more reliable means of sex estimation are not available during medicolegal examination.

Aims: To find out whether 2D:4D ratio of Madhya Pradesh region shows sexual dimorphism in both right and left digit ratio measuring dermatoglyphics lengths.

Materials and Methods: A total of 620 adults (310 males and 310 females) of the age group 18-25 were studied. The length of the index and ring finger were measured and 2D:4D ratios were calculated and statistically analyzed.

Results: There was a significant difference ($P < 0.0001$) in 2D:4D ratio with an overall accuracy of 83.55%. The final result of the analysis shows that 85.8% of males and 81.3% of females were sexed correctly.

Conclusion: We conclude that 2D:4D ratio is sexually dimorphic and suggests that the 2D:4D ratio is a constant feature among different age groups in different population.

Key words: 2D:4D ratio, Digit ratio, Prenatal androgen exposure, Sexual dimorphism

INTRODUCTION

Identification of human remains is the key element in forensic investigations consisting of determination of age, sex and stature assessment and also comparison with ante mortem data from fragmentary and dismembered remains.[1] Morphological and anthropometric relationship that exists between different part of the body and sex of an individual has been of great interest to forensic experts, anthropologists, and medical scientist for a long time because of the increase in the cases of mass disasters, explosions and assault cases and other catastrophic events causing mass deaths.[1-3] It, therefore, implies that accurate sexing of human remains has the potential to narrow down the search to a particular sex and gives the right direction to the ongoing forensic investigation.[4,5] Studies have focused on the role of hand and foot measurements in establishing the biological profile of individuals in forensic investigation because the dismembered remains includes the terminal parts of the human body such as hands and feet in cases of mass disasters.[3,6-11]

Hand analysis has intrigued humans throughout history. In recent times two aspects of human hand have drawn attention for observation and analysis including dermatoglyphic ridge pattern and secondly, finger lengths and their ratios.[12] Besides the lengths of the fingers such as index finger length and ring finger length, finger ratios have also been used for predicting sex of an individual. The finger ratio is an established sexually dimorphic biometric population marker.[13-15] This ratio is negatively related to prenatal testosterone and positively related to estrogen. If 2nd and 4th digit (2D:4D) in adults is a correlate of prenatal sex steroids we should expect it to be sexually dimorphic, the dimorphism should be present in young children and once established in early neonatal life digit ratio assumed

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to be stable in later life[16-18] and it is genetically controlled by the HOX genes which also control the differentiation of the urogenital system and may, therefore, indirectly influence the prenatal production of testicular androgen and the development of the digits.[16,19] There is evidence that sexual dimorphism in digit ratios develops in utero between the 13th and 14th week of gestation,[16,20,21] under the influence of parental androgens and estrogens.[22,23]

It has been observed that India, as a country, consists of a large number of ethnic and indigenous elements, varied geographical conditions and these have enormous amounts of ethnic and genetic diversity[4,5] which differ with race, sex and geographical locations.[24] Literature on the index and ring finger ratio in sex prediction has shown variable results in terms of its forensic significance. It is observed that the index finger length and ring finger length ratios differ between populations and its utility appear to be limited in forensic case work.[17,25] Apparently, the need to estimate sex of an individual using a part of the hand or fingers arises when only part of a hand is available for examination. Such studies are lacking for one of the largest indigenous populations of India.[9] Therefore, there is a need for regional studies in the process of identification of human remains as the human species inhabit diverse environments all over the earth and exhibit a lot of racial and ethnic variations.

The purpose of this study is to extend the research in the people of Madhya Pradesh as to best of our knowledge to encourage the work on different population and also the study group includes a larger number of subjects than the previous studies so that the results of statistical calculation can be as accurate as possible. As per above, this study has been undertaken to investigate sexual dimorphism in the lengths of index and ring fingers and to derive models for estimating sex using these measurements and to confirm 2D:4D as a proposed faithful postnatal biomarker for gestational exposure of testosterone.

MATERIALS AND METHODS

This study was conducted on 620 individuals (310 males and 310 females) residing in MP. India for at least two generations, belonging to age group of 18-25 years having no disease or deformity of the digits which were measured anthropometrically in respect to their sex and digit lengths 2D:4D. The subjects were Medical, Dental, and Physiotherapy students of Government Medical Colleges of Madhya Pradesh.

Methodology

Dermatoglyphic lengths of 2D:4D of both hands were taken and their ratios were calculated. The length was measured from proximal crease at the base of the finger to the tip of the finger in the midline on the palmar aspect of the hand using vernier calipers (Figure 1) without exerting pressure by a single experienced observer and protruding finger nails were excluded.[17] Prior informed written consent was obtained from each subject. Subjects were asked to remove any jewelry or rings that would interfere while obtaining the finger length measurements. Measurements were taken twice for accuracy and to take out mean in a well-lighted room.

Statistical Evaluation

Data thus were compiled, tabulated and analyzed statistically on Word Excel and SSP softwares. Descriptive statistics (mean ± standard deviation) of the 2D:4D for the left and right hands were tabulated for both males and females. Data obtained was analyzed using Student *t*-test and *P* values were calculated. Analysis of variance and discriminant function analysis were also done on the data.

RESULTS

Table 1 shows the mean value of lengths of 2D, 4D and 2D:4D ratio in the right and left hands in males and females obtained by measuring dermatoglyphics lengths using vernier calipers. The sex differences for all parameters were highly significant ($P < 0.001$).

The Graph 1 compares the 2D:4D ratio in the right and left hands of both males and females with mean 2D:4D ratio of 0.973 in males as compared to 2D:4D ratio of 1.01 in females.

Statistical calculations of males and females have been summarized in Table 2, which shows comparison of mean of 2D:4D ratio in the right and left hands of both males and females. Students *t*-test and analysis of variance have

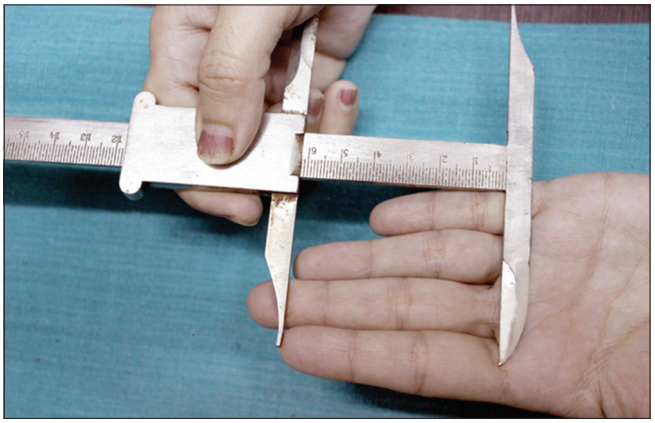


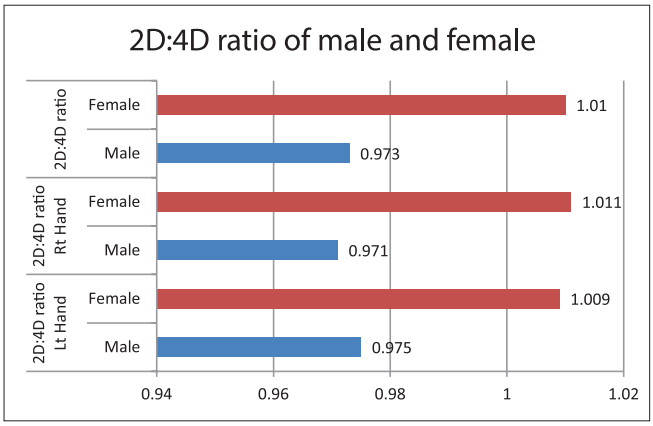
Figure 1: The measurement of index finger using vernier calipers

been applied and *P* values and *t* values were calculated which were highly significant (<0.05) in terms of sexual differences.

By discriminant function analysis it was found that 2D:4D ratio could be used to study sexual dimorphism with an overall accuracy of 83.55%. The final result of the analysis shows that 85.8% of males and 81.3% of females were sexed correctly.

DISCUSSION

Sexual dimorphism in the absolute length of fingers has been demonstrated in various studies.[3,26-28] The morphological gender difference has been reported with male fingers being significantly longer as compared to female fingers.[3,14,26-29] In females, the index and ring fingers tend to be almost of equal length, whereas in males the ring finger tends to be much longer than the index finger. The 2D:4D ratio is lower in men as compared to women. Lower index and ring finger ratio have been considered "masculine" and higher ratios as "feminine." Thus, the index and ring finger ratio becomes a significant parameter for determining sex.[3,26] The sex difference in 2D:4D ratio is independent of the body size, as it is not significantly related to the height and age in either sex.[14,27,29] The 2D:4D ratio as a sexually dimorphic trait is established early in life and remains fairly stable postnatal; it does not change with age and growth in a population group.[17,25,30,31] High concentrations of fetal testosterone indicate a low 2D:4D ratios, which, therefore, indicate a high prenatal testicular activity. On the other hand, 2D:4D is positively correlated with estrogen in men and women.[23,28,32]



Graph 1: 2D:4D ratio of male and female

Table 1: Statistics of 2D and 4D of right and left hand of male and female

Parameter	Males (*n*=310)	Females (*n*=310)	*P*
2D right	7.19±0.33	6.61±0.33	0.000
2D left	7.24±0.35	6.61±0.34	0.000
4D right	7.41±0.31	6.54±0.32	0.000
4D left	7.43±0.33	6.55±0.35	0.000
2D:4D right	0.97±0.03	1.01±0.03	0.001
2D:4D left	0.97±0.03	1.01±0.03	0.001
Mean 2D:4D	0.97±0.02	1.01±0.03	0.000

2D: Length of index finger, 4D: Length of ring finger, *n*: Number of subjects

Besides sexual dimorphism, index and ring finger ratio shows significant ethnic and population differences.[30,33] The extent of sex differences, however, varies in different studies and population groups. A number of studies have reported the existence of significant sex differences in 2D, 4D and its ratio in different ethnic populations and its bilateral variations among individuals belonging to different Indian ethnic groups.[13-15,26,27,29] Considerable overlapping in the frequency distributions of index and ring finger ratios were observed among both sexes in the study population. In general, a lower IFL and RFL ratio has been reported among females.[14,29,34,35] In this study, 2D:4D ratio in females is significantly higher than males in both hands. This observation agrees with earlier reports as by many authors.[27,36-39]

Our study confirms the observations of other researchers that the sex differences in the index and ring finger ratio can be a useful sex indicator especially when DNA analyses cannot be performed.[40] In this study, males show higher mean values in each anthropometric dimension than among females. These statistically significant differences may be attributed to the early maturity of girls than boys;

Table 2: Statistics of 2D:4D ratio of male and female

Statistics	2D:4D ratio right hand		2D:4D ratio left hand		2D:4D ratio	
	Male	Female	Male	Female	Male	Female
Mean	0.9708	1.0111	0.975	1.0088	0.973	1.0100
SD	0.0264	0.0339	0.0267	0.0284	0.0250	0.0269
95% confidence interval	0.9708±0.0043	1.0111±0.0055	0.9734±0.0043	1.0088±0.0046	0.9721±0.0040	1.0100±0.0043
P value (two-tailed)	1.25×10^{-25}*		3.05×10^{-24}*		1.53×10^{-29}*	
Are means significantly different? (*P*<0.05)	Yes		Yes		Yes	
t value	*t*=11.52		*t*=11.16		*t*=12.62	
F value	132.61		123.54		159.27	
Pooled variance	0.0009		0.0008		0.0007	

*Significant. SD: Standard deviation

consequently, the boys have 2 more years of physical growth. The difference with other studies can be attributed to the population and ethnic differences between the study population and the other earlier studies. Our study is consistent with the early hypothesis that fetal hormones affect 2D:4D ratios.[23,38,39,41,42]

There are some limitations of this study. As this study is conducted on live adult population, the findings of this study thus, should not be applied on children, adolescents, and elderly individuals. The dimensions of fingers are likely to alter after death with rigor setting in and with putrefactive changes occurring later. Therefore, the observations of this study can be applied only in the human remains that are relatively fresh and not having post-mortem changes. The findings may not be suitable for dry, decomposed and bloated bodies that affect hand dimensions.

CONCLUSION

It is concluded that the sexual dimorphism of 2D:4D ratio is a constant feature among different age-group in different populations. The 2D:4D ratio is smaller in human males than in females. Estimation of sex from 2D:4D ratio is a supplementary approach when extremities or other body parts are not available for examination. This study has highlighted the application of 2D:4D ratio to determine sex among individuals belonging to the Madhya Pradesh population of India when more reliable means of sex estimation are not available during medicolegal investigations; also useful for human biologists and physical anthropologists for determination of sex from the fragmentary remains of hand and also in ergodesign applications of hand tools and devices. Studies on estimation of sex from finger lengths in different age groups and among different populations and ethnic groups need to be encouraged. No particular ethnic groups have been included, in the study, but combinations of variegated ethnic groups are considered. Therefore, this study has better applicability when applied on the same population.

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Original Article

Distribution of Causes of Abnormal Uterine Bleeding According to Polyp Adenomyosis Leiomyoma Malignancy and Hyperplasia Coagulopathy Ovulatory Dysfunction Endometrial Latrogenic not yet Classified Classification in a Tertiary Care Center

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Abstract

Introduction: Abnormal uterine bleeding (AUB) is defined as bleeding from uterine corpus that is abnormal in volume, regularity and timing. AUB affects 5-15% of women in reproductive age group. The Federation of Gynecology and Obstetrics in 2011 has introduced a newer classification system called PALM-COEIN for simplifying stratification of patients and help them in approaching treatment modalities.

Aims and Objectives: The aim of the study is to categorize women with AUB based on PALM-COEIN classification in a tertiary care hospital, Mysore Medical College and Research Institute.

Materials and Methods: The study material includes all women with AUB attending gynecology outpatient department from June 2016 to August 2016. It is a retrospective study.

Results: A total of 50 cases were studied during this period. The distribution of cases according to PALM-COEIN was polyps- 4%, adenomyosis- 6%, leiomyoma- 70%, malignancy- 6%, ovulatory dysfunction- 2%, endometrial- 6%, and not yet classified- 6%.

Conclusion: In our hospital fibroids are comprising the major cause of AUB followed by malignancies. This classification system helps us in the specific management of a broad group of disorders included under AUB.

Key words: Abnormal uterine bleeding, Intermenstrual bleeding, Polyp adenomyosis leiomyoma malignancy and hyperplasia coagulopathy ovulatory dysfunction endometrial latrogenic not yet classified

INTRODUCTION

Abnormal uterine bleeding (AUB) is a common cause of concern among women of reproductive age group and as well as a frequent cause of visits to the gynecology outpatient departments and/or health-care providers. Menorrhagia affects 10-30% of the menstruating women, and many occur during the perimenopause in up to 50% of the women.

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AUB defined as bleeding from the uterine corpus that is abnormal in regularity, volume, and frequency or duration that occurs in the absence of pregnancy.[1] Because of the growing concerns and facing difficulties in designing multinational clinical trials and in interpretation of isolated research studies using these terminologies, the need for

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simpler terms with clear meanings was recommended that have a potential to be understood by health professionals and patients alike and that can be translated into most languages.[2] According to the suggestion of publication in 2007, a process was designed that leads to international agreement on terminologies and definitions that were used to describe the abnormalities of menstrual bleeding.[3] Then, all the abnormalities in uterine bleeding are considered one term AUB. In 2011, to standardize the terminology, diagnosis, and investigations of the causes of AUB, a new system for the classification of AUB as the International Federation of Gynaecology and Obstetrics (FIGO) classification system was approved by the FIGO executive board.[3,4] An internal group of clinicians investigators from six continents and over 17 countries contributed to bleeding abnormalities in it in an effort to create universal accepted system of nomenclature to describe uterine reproductive aged women, an leiomyoma, malignancy and hyperplasia, coagulopathy, ovulatory dysfunction, endometrial, iatrogenic and not yet classified known by the acronym PALM-COEIN was published alternative classification system, polyp, adenomyosis, in 2011 by the International FIGO and adopted by the American college of obstetrics and gynecologists (Table 1).

The term dysfunctional uterine bleeding often used synonymously with AUB in the literature to indicate AUB for which there was no systemic or locally definable cause is not part of the PALM COEIN system and discontinuation of its use is recommended.[5]

By using this system, the possibility of the contribution of more than one pathology in an individual symptomatic woman and also a lack of contribution of a coincidental asymptomatic pathology toward AUB due to other causes can be recognized. This system will facilitate multi-institutional investigation in to the epidemiology, etiology and treatment of women and acute and chronic AUB.

MATERIALS AND METHODS

The retrospective study includes all women of reproductive age with AUB attending gynecology outpatient department (OPD) from June 2016 to August 2016.

Inclusion Criteria

- Women between menarche to menopause
- History of irregular menses with excessive bleeding for prolonged duration.

Exclusion Criteria

- Women with cervical cause for vaginal bleeding
- Pregnant women with bleeding.

Table 1 : Palm coein classification

Structural causes	
P	Polyp
A	Adenomyosis
L	Leiomyoma
M	Malignancy and hyperplasia
Non structural causes	
C	Coagulopathy
O	Ovulatory dysfunction
E	Endometrial
I	Iatrogenic
N	Not yet classified

This study comprises 50 women of reproductive age with AUB either in duration, volume, or in frequency for at least 3 months presenting to OPD of Mysore Medical College and Research Institute, Mysuru, India from June 2016 to August 2016.

These patients underwent history, detailed physical and local examination, necessary blood investigations, and pelvic ultrasonography. Endometrium and hysterectomy specimens were obtained for histopathology if needed. According to the polyp adenomyosis leiomyoma malignancy and hyperplasia coagulopathy ovulatory dysfunction endometrial latrogenic not yet classified (PALM-COEIN) classification system, the possible causes were identified, and the patients were categorized accordingly. Patients identified with polyp, adenomyosis, and leiomyoma after per speculum and per vaginal examination followed by ultrasound were categorized under AUB-P, AUB-A, and AUB-L, respectively. Bleeding due to endometrial carcinoma diagnosed after either endometrial biopsy or hysterectomy on histopathological examination was included under AUB-M category. Patients taking anticoagulants and with defects of coagulation from younger age were grouped under AUB-category C.[4]

Bleeding with unpredictable, irregular timing and variable in amount was suspected to be due to ovulatory dysfunction and categorized under AUB-O. When abnormal menstrual bleeding occurred in the cyclical and predictable pattern, typical of ovulatory cycles and no other cause is identified, it was considered as a disorder of endometrium and was placed under AUB-E. Patients presenting with abnormal bleeding due to gonadal steroid hormonal intake during the preceding 3 months or due to the usage of inert or medicated intrauterine device was categorized as iatrogenic and grouped under AUB-I. Women not fitting into any category were put under not yet classified category, i.e., AUB-N.

RESULTS

In this study, 50 patients were included after fulfilling all the inclusion criteria. All these cases were placed in

Table 2: Distribution of cases of AUB

Causes of AUB	Number of cases (%)
Polyp	2 (4)
Adenomyosis	3 (6)
Leiomyoma	35 (70)
Malignancy/hyperplasia	3 (6)
Coagulopathy	0
Ovulatory dysfunction	1 (2)
Endometrial	3 (6)
Iatrogenic	
Not yet classified	3 (6)

AUB: Abnormal uterine bleeding

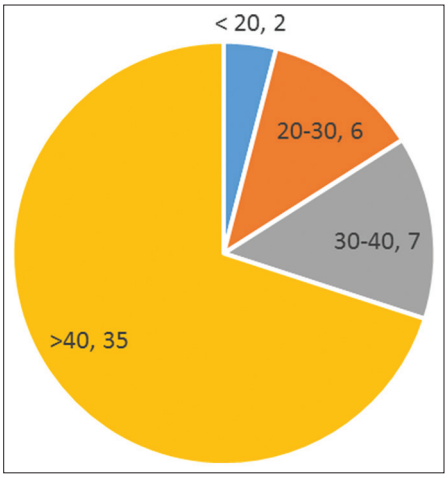

Figure 1: Age distribution of cases

the nine categories of the PALM-COEIN classification. Maximum patients were in the age group of 40-49 years (70%) (Table 2). The most common presenting complaint was heavy menstrual bleeding.

Distribution of Causes of AUB in Present Study According to PALM-COEIN Classification

After classifying the patients according to PALM-COEIN classification, it was found that leiomyoma was the most common cause of AUB in patients presenting to the gynecology OPD (70%). It was followed by malignancy (6%), adenomyosis (6%), endometrial causes (6%), not classified (6%), polyp (4%), and coagulation abnormalities contributing least to the classification.

DISCUSSION

AUB in women of reproductive age is a manifestation of any of a number of disorders or pathologic entities. The absence of a universally accepted method for the classification of AUB has impeded basic science, clinical investigations, and practical applications of medical and surgical therapy.[3] Hence, adoption of new terminologies in clinical practice is needed for the effective management of AUB. A useful interpretation of results of various clinical and basic science research studies aiming at determining epidemiology, etiology, treatment, and prognosis of AUB was hampered due to a lack of consistent classification.

This study primarily focused on categorizing the patients of AUB according to the PALM-COEIN classification similar to the studies done by Munro *et al.*,[6] Priyanka *et al.*,[7] Bahamondes *et al.*,[3] Goel *et al.*,[8] and Gouri *et al.*[9] so that planning, investigations, and treatment can be easier and done in a proper way. Most of the patients who presented with AUB in gynae OPD were in the age group 40-49 years (70%), and the most common presenting complaint was heavy menstrual bleeding (Figure 1).

According to the study conducted by Qureshi and Yusuf[10] in 2013, maximum patients of AUB were classified under leiomyoma category, the number being 25% followed by ovulatory dysfunction (24%). Whereas, in a study conducted by Gouri *et al.*,[6] in May 2016, the maximum number of patients were categorized under ovulatory dysfunction (27%) and followed by leiomyoma (24.67%). Similarly, in this study also, leiomyoma (70%) was found to be the most common cause of AUB followed by malignancy and adenomyosis (6% and 6%, respectively) (Table 1).

CONCLUSION

The new PALM-COEIN classification system for AUB approved by a multinational group of clinicians and investigators is expected to facilitate proper and easier diagnosis of etiology and treatment of women with acute and chronic AUB. To reach a precise underlying etiology is imperative for successful treatment of AUB. However, it is recognized that this system requires periodic modification and occasional substantial revision depending on advances in knowledge and increasing availability of investigative options.

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Review Article

Sertoli-Leydig Cell Tumor of Ovary, Management and Prognosis: A Review of Literature

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Abstract

Sertoli-Leydig cell tumor of ovary is a rare type of sex-cord stromal tumor. Only few case reports are published in the literature. The majority of the cases occur in young women and are benign and unilateral in location. Nearly, 30-40% of the patients present symptoms and signs of virilization. In most of the cases, histopathologically, the degree of differentiation is intermediate or poor. Majority cases are diagnosed at Stage I and extraovarian spread at the time of diagnosis are very uncommon. The degree of tumor grading/differentiation and staging are important prognostic factors. The rarity of the tumor results in inadequate data regarding management protocol. Surgery is the important initial treatment part. Chemotherapy is indicated in the presence of poor prognostic factors, but, controversy exists. There is a need for more number of studies for a standard treatment protocol including chemotherapy.

Key words: Chemotherapy, Heterologous elements, Ovary, Sertoli-Leydig cell, Surgery, Virilization

INTRODUCTION

Sex-cord stromal tumor consists of granulose, thecal cells, and fibrocytes, derived from stromal component of ovary and testis. It consists of 8% of ovarian cancers and 5% of testicular cancers. The classification is based on the cell/tissue type, i.e., sex-cord, gonadal stroma, and mixed. Granulosa cell tumor, thecoma, fibroma, Sertoli cell tumor, Leydig cell tumor, Sertoli-Leydig cell tumor (SLCT), and gynandroblastoma are the various types of sex-cord stromal tumors. Among these, SLCT consists of 1% of sex-cord tumors. The site of occurrence, i.e., ovary is an extremely rare entity constituting <0.5% of all ovarian neoplasms.[1,2] Although both the Sertoli and Leydig cells are found in the testicle, this tumor can occur in ovary. The majority are presented at young age group (20-40 years age group). SLCTs are usually unilateral at the time of presentation, and bilateral presentation is seen in only 2% of cases.[3] Symptoms and sign of presentation depend on mass occupying lesion or excess hormonal production.[2,4-6] The aggressive nature of the tumor depends on the degree of differentiation on histopathology.[7] Approximately, 90% of the cases are diagnosed at Stage I.[8] A combination of both histopathology and immunohistochemical examination results in more accurate definitive diagnosis of SLCTs.[9]

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DEFINITION

Ovarian sex-cord stromal tumors are a heterogeneous group of neoplasms developing from the stem cells furnishing around the oocytes including the cells producing hormones. The World Health Organization (WHO) classified ovarian sex-cord stromal tumors into four groups such as: Granulose cell tumor, Sertoli-stromal cell tumor, mixed or unclassified type, and steroid cell tumors. SLCT is included under Sertoli-stromal cell tumor. Nowadays, the terminologies such as arrhenoblastoma and androblastoma are replaced by SLCTs. The WHO definition of SLCT is the tumor composed of variable proportions of Sertoli cells, Leydig cells, and in the case of intermediate and poorly

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differentiated neoplasms, primitive gonadal stroma, and sometimes heterologous elements.[10]

CLINICAL FEATURES

Most of the epithelial ovarian SLCTs present at advanced stage whereas sex-cord stromal tumors/SLCTs diagnosed at early stage and with low-malignant behavior. It can occur at any age group between 2 and 75 years. However, majority present at young age with the average age of presentation is 25 years. Symptoms and signs are related to either mass effect or due to excess hormone production. Nearly, 50% of the patients are presented with lower abdominal or pelvic mass with pain due to pressure effect of the mass.[2,5,6] SLCT masses are usually mobile, unilateral, and detected by self or clinical examination.[4] Pain is usually chronic and dull in nature due to capsular expansion and pressure effect on surrounding visceral structures.[4] 15% of the cases are presented with acute abdominal pain due to ovarian torsion, capsular rupture, and bleeding.

More than 50% of the patients are with excess androgen production and presents with virilism, hirsutism, acne, alopecia, breast atrophy, hoarseness of voice, clitoromegaly, and amenorrhea.[4] Patients rarely present with precocious puberty, abnormal uterine or vaginal bleeding, generalized edema, breast hypertrophy, weight gain, endometrial hyperplasia due to estrogen excess production.

Feminine features improved after surgery, whereas, consequence of masculinization disappears slowly.

PATHOLOGY

Morphologically, SLCT resembles the cells of testis under various stage of development, but, ultrastructurally, resembles ovarian granulose cell tumor. Various degrees of differentiation or grading found in SLCTs such as well, intermediate, and poorly differentiated.[11] Both intermediate and poorly differentiated forms are mostly seen. Heterologous elements are found in 20% of cases and include both endodermal and mesenchymal elements.[12] The endodermal elements show both gastric and/or intestinal type of mucin-secreting epithelium, and the mesenchymal elements show immature cartilage, bone, smooth muscle, and skeletal muscle. Endodermal elements are usually associated with intermediate differentiation whereas mesenchymal elements are commonly associated with poorly differentiation and sarcomatoid background.[13] Approximately, 50% of cases come to clinical attention because of progressive defeminisation.[2]

SCLTs are typically well encapsulated solid, firm, lobulated yellow or tan tumor with smooth external surface. Cut section shows greasy/fleshy consistency, straw-colored fluid, and cystic spaces, but necrosis and hemorrhagic areas are less common and mostly seen in poorly differentiated histopathology. Microscopically, there is varying degree of differentiation of tubules lined by Sertoli cells and intervening nests of Leydig cells.[14] Well and intermediate differentiated types have Leydig cells in clusters in interstitial stroma, and Sertoli cells forming tubular structures and mitotic figures are very rare. Poorly differentiated forms lack a classical arrangement between tubules, Sertoli cells, and Leydig cells and the tumor cells have immature differentiation, high nuclear atypia, increased nuclear to cytoplasmic ratio, coarse chromatin, and abundant mitotic figures. In addition, reticular form found in 10% of cases, and microscopically, it is typical, a network of slit-like spaces and cysts containing papillae. Immunohistochemical examination shows positivity for inhibin and calretinin and negative for epithelial membrane antigen.[15] Low-molecular weight cytokeratin (AE1/AE3), CAM5, WT-1, and CD56 markers may be positive.[16,17]

SERUM MARKERS

About 80% of patients with ovarian SLCTs present with increased level of serum testosterone and androstenedione.[18,19] There is increased production of androgen (40% of cases), whereas, excess estrogen production is rare. Inhibins are normally secreted in granulose and Sertoli cells of the ovary, and increased serum levels may be seen in SLCTs.[20-23] Increased serum testosterone level more than 200 ng/dl are commonly found in androgen secreting neoplasm from ovaries or elsewhere.[24] Total inhibin is a sensitive immunohistochemical marker for ovarian sex-cord-stromal tumors.[25,26] Paracrine action of inhibin at theca cells may enhance androgen production.[27]

RADIOLOGICAL INVESTIGATION

During the period of clinical diagnosis of SLCTs, extraovarian spread is rarely seen accounting for 2-3%.[2,5,6]

Ultrasound

Transvaginal ultrasound is the best initial imaging method for the assessment of SLCTs and typically exhibit solid appearance.[4,28] It has high sensitivity, cost-effectiveness, and yields better morphological features of adnexal mass in comparison to abdominal ultrasound.[29] SLCTs may be purely cystic, purely solid, or mixed.[30] It typically shows a solid mass with intramural cystic component. Ultrasound does not rule out the diagnosis of ovarian SLCT in situation of excess androgen, and estrogen.[4] Highly vascular nature of the tumor on color Doppler study suggests malignant nature of the lesion.

Computed tomography, magnetic resonance imaging (MRI), and positron-emission tomography scans are used for better characterization of the primary tumor, detection of locoregional spread, distant metastasis and possible second primary.

Pelvic MRI

The signal intensity of T2-weighed MRI depends on the fibrous component of SLCTs. SLCTs usually has low signal intensity on T2-weighed MRI with few areas of high signal intensity.

Prognosis

The tumor stage (extent) and degree of differentiation (grading) are the most important prognostic factors.[2] The previous study showed well-differentiated (Grade-1) SLCTs were benign, whereas, 11% of tumors with intermediate differentiation (Grade-2) and 59% of poorly differentiated tumors and 19% of cases with heterologous elements were malignant.[2] Local recurrence rarely occurs in well-differentiated early stage SLCTs. Metastasis can occur to omentum, abdominal lymph nodes, or liver, and less likely to lungs, bone, brain, and other parts. The 5-year overall survival is different according to degree of differentiation: 100% in well-differentiated SLCTs and 80% in Grade-2 and Grade-3 patients.[31] The overall 5-year overall survival for Stage I is 95%, whereas, it is zero percent for Stage III and IV patients.[2,5]

Treatment

Till date, there are only a few cases reported in the literature regarding ovarian SLCTs and the insufficient data resulted in lack of standard treatment protocol guidelines.[32] Surgery is the initial treatment of choice in ovarian SLCTs.[9] Adjuvant chemotherapy is still controversy due to inadequate data.

Tumor staging is necessary to know the prognosis of the SLCTs and to guide for further management. Most of the cases are unilateral and diagnosed at Stage I without any extraovarian spread. Therefore, conservative surgery is an appropriate treatment in young patient. Unilateral salpingo-oophorectomy is the preferred surgical method in young woman with stage disease.[33] Few literature reports successful management of ovarian SLCTs by laparoscopic surgery.[34] Adjuvant chemotherapy should be considered in Stage I patient with the presence of risk factors: Intermediate and poorly differentiated tumors, heterologous elements, increased mitotic rate, rupture or spillage of the tumor, and advanced stage/metastatic tumor of any histologic type.[2,5,6,33] Tumor with Stage II or higher, should be treated with total abdominal hysterectomy (TAH) and bilateral salping-oohprectomy (BSO) plus staging surgery (omentectomy, appendectomy, and pelvic lymphadenectomy) followed by adjuvant chemotherapy. Fertility-sparing surgery can be done in patients with well-differentiated histology, but in Grade-2 and Grade-3 patients, unilateral salpingo-oophorectomy with standard staging surgery should be performed.[33,35] Treatment with pelvic lymphadenectomy is still questionable. However, pelvic lymph node metastasis in SLCT is extremely rare and pelvic lymphadenectomy may be excluded from staging surgery.[36] Elder age group or patient with progressive disease should be treated with complete surgery, i.e., TAH plus BSO with omentectomy, appendectomy, and pelvic lymphadenectomy.[17] Combination chemotherapy with BEP regimen (bleomycin, etoposide, and cisplatin) is the most frequently used first-line chemotherapy regimen.[37] Other chemotherapeutic regimens used in SLCTs are CAP (cisplatin, adriamycin, and cyclophosphamide) and PVB (cisplatin, vinblastin, and bleomycin).[38] However, due to rarity of the tumor and less number of reported data, the role of adjuvant chemotherapy is still questionable.

CONCLUSION

SLCT is an uncommon variety of ovarian sex-cord tumor, and most of the cases found unilaterally, present at Stage I, extraovarian spread and lymph node involvement are uncommon. Young female with symptoms of virilization and presence of ovarian mass clinicoradiologically should be considered as SLCT unless otherwise proved. Management is solely based on histopathology and staging/extent of the tumor. Patient desiring fertility is an important issue in the management of SLCTs. Stage I patients should be treated with conservative surgery. Adjuvant chemotherapy should be given in poorly differentiated histology. Adjuvant chemotherapy in intermediate variety is individualized. Stage II or more than it should be treated with TAH plus BSO with standard surgical staging. However, due to rarity of the case, limited research data, there is no standard treatment guidelines regarding surgery and the role of chemotherapy and requires further evaluation.

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Case Report

Overlap/Diagnosis by Seclusion: A Case Report

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Abstract

A 32-year-old male diabetic patient presented with dry cough, hemoptysis, joint pains for 2 months. He had clinical features suggestive of both sarcoidosis (bilateral hilar adenopathy, negative Mantoux test, noncaseating granuloma in transbronchial lung biopsy) and tuberculosis (bronchial aspirate polymerase chain reaction positive for mycobacteria). This case report highlights the diagnostic dilemma between tuberculosis, sarcoidosis, and combined tuberculous sarcoidosis and the challenge physician has to face in managing such a patient with concomitant diabetes mellitus.

Key words: Diabetes mellitus, Sarcoidosis, Tuberculosis, Tuberculous sarcoidosis

INTRODUCTION

Classically sarcoidosis is known to be prevalent in a community coming out of the scourge of tuberculosis. However, it has been documented now that sarcoidosis can precede tuberculosis, follow tuberculosis or even coexist with tuberculosis. There is good evidence now to support the theory that mycobacterium tuberculosis is causally related to sarcoidosis. This presentation is an attempt to emphasize the need to differentiate undisputed tuberculosis or sarcoidosis or to define the overlap tuberculous sarcoidosis and the management when coexisting with diabetes mellitus.

CASE REPORT

A 32-year-old Asian male patient presented with dry cough and joint pains for 2 months and three bouts of hemoptysis in last 1½ months. He worked as a chef in UK and was an occasional smoker and social drinker. No other significant past or family history. To start with he developed running nose, fever, myalgia with one episode of loss of consciousness without any seizures while residing in UK. He was admitted in a hospital where his diabetic status was first detected. He was managed as lower respiratory tract infection with oral amoxicillin with clavulanate and metformin. Following improvement he was discharged after 3 days of hospitalization. A month later he traveled back to India and presented to us with above complaints. At presentation his vitals were stable. He was an average built man, no positive general examination findings. His blood investigation reports were total leukocyte count - 11,400/μl, DC-N 62%, L 33%, E 5%, erythrocyte sedimentation rate (ESR) 90/1st h, widal test positive (1/80), fasting blood sugar test 119 mg/dl, postprandial blood sugar 180 mg/dl, hemoglobin A1c 7.2%. Rest investigations within normal limits. Chest radiograph showed bilateral hilar lymphadenopathy (Figure 1). Spirometry within normal limit. Chest computed tomogram revealed right paratracheal, pretracheal, paraaortic, and bilateral hilar lymph nodes enlargement with linear reticular shadows in bilateral lung parenchyma suggesting diagnosis of sarcoidosis, but tuberculosis was kept in differential diagnosis (Figure 2). Sputum for acid fast bacilli was negative both in spontaneous as well as induced samples. Bacterial culture of the sputum showed no growth. Serum angiotensin converting enzyme was high (103 U/L); serum calcium 2.2 mmol/L, 24 h urine calcium level normal. Tuberculin skin test (10 TU) was negative. Ultrasound of abdomen showed mild splenomegaly and fatty liver. No cutaneous or opthalmological abnormality. Fiberoptic bronchoscopy showed extrinsic compression of carina, bilateral main

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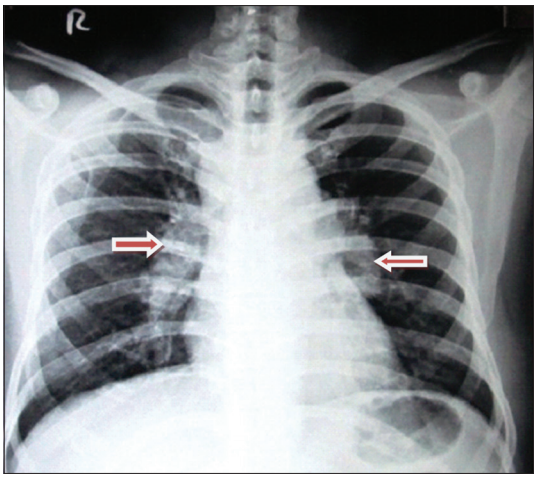

Figure 1: Chest X-ray showing bilateral hilar adenopathy (arrows)

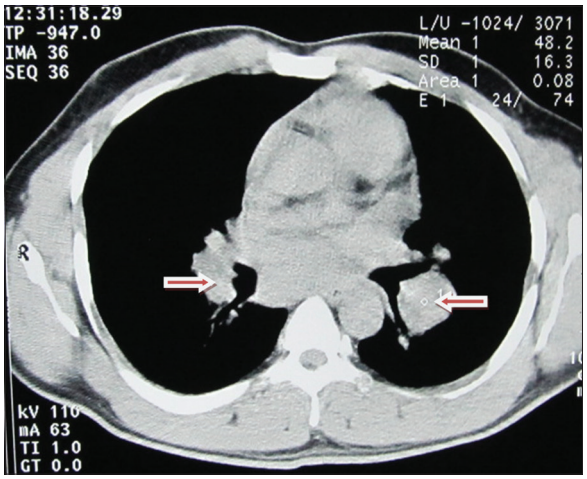

Figure 2: Computed tomography chest showing bilateral hilar adenopathy (arrows) – "Potato nodes" appearance

bronchi, and mucosal inflammation. Transbronchial lung biopsy showed noncaseating granuloma, bronchial aspirate positive for mycobacterium tuberculosis by polymerase chain reaction (PCR) method. A diagnosis of tuberculous sarcoidosis was made. Antitubercular therapy was started along with insulin for optimal glycemic control and other supportive treatment. Steroids were avoided considering the diabetic status. His clinical status, as well as radiologic picture, improved significantly after 2 months of therapy. Subsequently, he was lost to follow-up.

DISCUSSION

The term tuberculous sarcoidosis was first proposed by Scadding in the year 1962 for patients having clinicopathological features of both tuberculosis and sarcoidosis.[1] Pathogenesis of sarcoidosis has been a matter of intense scrutiny since long and till now it's not exactly known; but role of *Mycobacterium tuberculosis* has been increasingly supported.[2] Combined tuberculosis and sarcoidosis or tuberculous sarcoidosis can present in three patterns: (a) Patient of tuberculosis developing sarcoidosis later, (b) patient having coexistent tuberculosis and sarcoidosis, (c) patient of chronic sarcoidosis developing overt tuberculosis later. Shah *et al.* has proposed diagnostic criteria for tuberculous sarcoidosis and consider this as a transition of evolution of sarcoidosis from tuberculosis.[3,4] The salient points of these criteria are raised ESR, raised SACE, tuberculin test positive/negative, sputum positive/negative for *M. tuberculosis*, culture negative for tuberculosis, PCR of biopsy tissue positive for *M. tuberculosis*, chest X-ray bilateral hilar, right paratracheal lymphadenopathy, micro or macronodules in computed tomography scan of chest, no expected response to antitubercular therapy. However, the authors suggested these criteria should be considered open for modification.

CONCLUSION

In Asians more so in Indians with high incidence and prevalence of tuberculosis such concomitant presence of noncaseating granulomas, raised SACE levels, negative tuberculin test, PCR positivity for *M. tuberculosis* with mediastinal lymphadenopathy raise the possibility of coexisting tuberculosis and sarcoidosis. Furthermore, this supports the hypothesis of mycobacterial species, and it's components inducing pathological changes and clinical manifestations of sarcoidosis.

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Case Report

Peutz-Jeghers Syndrome: A Rare Case Report

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Abstract

We report a case of 26-year-old male presenting with features of intestinal obstruction which on ultrasonography was S/O intussusception. On examination, patient was having distended abdomen with generalized tenderness and guarding and multiple pigmented spots over his face, arms, and other parts of the body. On exploratory laparotomy, intussusception was found with ileum and jejunum as intussusceptum and colon as intussuscepien. On resection of jejunum and ileum multiple polyps were found which on histopathological examination were found to be hamartomatous polyps. Upper giscopy also showed polyps in different parts of stomach. These polyps with melanoma cutaneous pigmentation suggest a diagnosis of Peutz-Jeghers syndrome. This syndrome is a rare entity with patients having increased chances of intestinal and extra intestinal malignancy and hence should be subjected to regular follow-up with screening for other malignancies.

Key words: Hamartomatous polyp, Melanoma cutaneous pigmentation, Peutz-Jeghers syndrome

INTRODUCTION

Peutz-jeghers is autosomal dominant syndrome characterized by hamartomatous gastrointestinal (GI) polyps (<100) and mucocutaneous melanin pigmentation. These polyps are 1 mm to 4 cm in diameter, mostly seen in jejunum and small bowel > colon. They can also occur at nose, bronchi, renal pelvis, and biliary tree.[1-3]

CASE REPORT

A case of 26-year-old male patient, presented with complain of severe colicky pain in whole of abdomen since 7-8 days associated with multiple episodes of vomiting and passing blood in stool for 2 days. There was no significant last history. His father suffered from GI malignancy and died in his forties, but the details of the malignancy were not available. Patient was having pallor and was malnourished (weight: 40 kg). On gross inspection, multiple pigmented spots present on face and digits of arms and legs, on bucco-oral mucosa, and on lips. Per abdomen was distended with generalized tenderness and guarding. There was a lump of 6 cm × 6 cm size present in left lumbar region extending into the umbilical region. On Per rectum examination stool mixed with blood with normal mucosa, and normal prostate size was found. Proctoscopy was normal with no visible pigmentation.

Blood investigations and X-ray chest were normal. X-ray abdomen standing was S/O multiple air fluid levels. Ultrasonography was S/O clumped small bowel loops in left hypochondrium and epigastric region P/O intussusception.

Intraoperative Findings

On opening peritoneum, jejuno-ileal type of intussusception was found which was reduced intussucipiens was found to be jejunum and some part of ileum and intussuceptum was distal ileum and colon. Most of the intussucipiens

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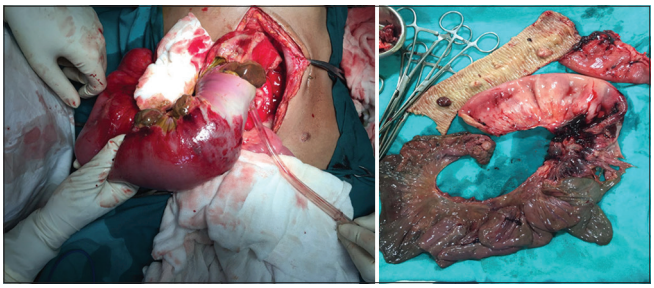
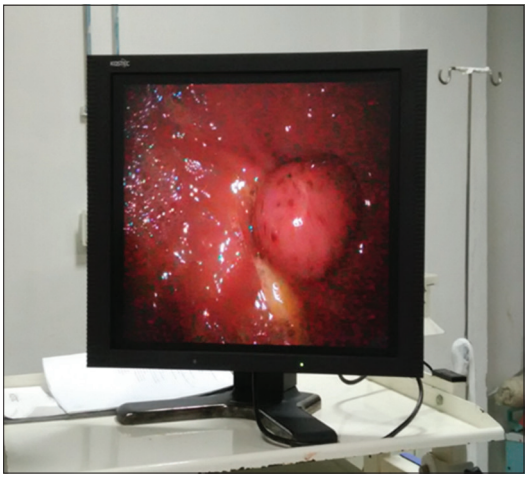
was gangrenous and sloughed out and was resected with jejuno-ileal anastomosis being done. Resected part had a number of polyps in its lumen which on histopathological examination was S/O hamartomatous polyps.



Hence postoperatively upper giscopy was done which revealed polyps in the distal part of stomach. Colonoscopy is awaited in this patient.



DISCUSSION

Peutz-jeghers is autosomal dominant syndrome characterized by hamartomatous GI polyps (<100) and mucocutaneous melanin pigmentation. These polyps are 1 mm to 4 cm in diameter, mostly seen in jejunum and small bowel > colon. They can also occur at the nose, bronchi, renal pelvis, and biliary tree. Pigmentation is seen in perioral, buccal mucosa, digits of hands and feet and perianal and genital region. These patients mostly present in 3rd decade with abdominal pain due to intussusception. Other less common presentations: Symptoms from obstruction of large polyps, anemia, hematochezia, hematemesis, biliary obstruction, and gastric outlet obstruction. They are at an increased risk of both GI and extra GI malignancy such as that of pancreas, breast, thyroid, lungs, gallbladder, ovary, and testes.[3-6]

CONCLUSION

Because of the increased malignancy chances, the patient is kept on regular follow-up with screening with intervention as and when required.

Screening Guidelines

Colon and rectum	Baseline colonoscopy at age 8
	If polyps detected, colonoscopy every 3 years until age 50
	If no polyps detected, repeat colonoscopy at age 18 and every 3 years after until age 50
	Continue surveillance at 1- to 2-year intervals after age 50
Small intestine	Baseline EGD at age 8
	If polyps detected, EGD every 3 years until age 50
	If no polyps detected, repeat EGD at age 18 and every 3 years after until age 50
	Continue surveillance at 1- to 2-year intervals after age 50
	Baseline video capsule endoscopy at age 8
	Repeat every 3 years
Genital tract	Annual testicular examination beginning at birth until 12 years
	Testicular ultrasound if abnormalities on examination
	Cervical smear with liquid-based cytology at age 25 years
	Repeat every 3 years
Breast	Monthly self-examination beginning at age 18
	Annual breast MRI from age 25 to 50
	Annual mammography beginning at age 50
General	Annual complete blood count and liver function tests
	Annual full physical examination

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