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Study of Functional and Radiological Outcome of Midshaft Clavicle Fractures Managed Operatively With Plating

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Abstract

Introduction: Clavicle is one of the commonly fractured bones. Shortcomings of conservative treatment are non-cosmetic bump in addition to non-union in few cases. Shortcomings of operative treatment are hypertrophic scar and hardware-related issues in addition to surgical site infection possibility. Hence, we decided to carry out prospective follow-up study.

Materials and Methods: A prospective follow-up study was done in 57 consecutive patients from February 2016 to January 2017 at MIMER Medical College, Talegaon Dabhade. Patients were operated with precontoured 3.5 mm dynamic compression plate over superior aspect of clavicle. Patients were followed up at 2, 4, 6, 12, and 24 weeks after operation.

Results: In our study, mean time for radiological union was 39.4 days only with operative treatment. In our study, only there was only one case of non-union of 51 patients were present (<2%). Overall, satisfaction rate after operative treatment was quite high in our study. There were hardware problems in 10 cases of 51 patients, that is, about 19.60% of cases. These included screw loosening (4 cases) and hardware prominence in 6 cases (i.e. 11.76%). Hypertrophic scar in 2 cases (3.92%) and infection in 1 case (1.96%) were seen. Range of motion of shoulder was near normal.

Conclusion: Open reduction and internal fixation of midshaft clavicle fractures give good functional and radiological outcomes with high patient satisfaction rate without any major complication.

Key words: Clavicle, Malunion, Non-union, Plating

INTRODUCTION

Clavicle is one of the commonly fractured bones which accounts for about 2–3% of all fractures and up to 40–45% of all fractures of the shoulder girdle fractures.^[1] In India, almost all clavicle fractures including displaced or comminuted ones are managed conservatively traditionally

even in the laborers or daily wage workers who rely on good shoulder function for their livelihood. However, there is 10–15% non-union rate in severely displaced or comminuted fractures if conserved according to literature.^[2] However, it is still not clear whether surgery produces better outcomes than non-surgical treatment.^[3] Robinson has classified clavicle fractures into three types based on their location along the bone. Fracture of middle third is about 70–80% of all these.^[4] Shortcomings of conservative treatment are non-cosmetic bump in addition to non-union in few cases.^[5] Shortcomings of operative treatment are hypertrophic scar and hardware-related issues in addition to surgical site infection possibility.^[6] Hence, we decided to carry out prospective follow-up study to evaluate the outcome of operative treatment of midshaft clavicle fractures.

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MATERIALS AND METHODS

A prospective follow-up study was done in 57 consecutive patients from February 2016 to January 2017 at MIMER Medical College, Talegaon Dabhade, provided patients fulfilled the inclusion criteria and gave informed consent before study to participate in the study. Appropriate ethical clearance was obtained. All patients were followed up regularly for 6 months. Of the original 57 patients, three did not follow-up, one sustained head injury, one sustained fracture of ipsilateral limb, and one died due to unrelated cause. Hence, only 51 patients remained in the study. Inclusion criteria were midshaft fractures in skeletally mature patients. We excluded patients with immature skeleton (<18 years age), open fractures, pathological fractures, associated head injury, neurovascular injury, or ipsilateral limb injury. Patients were operated with precontoured 3.5 mm dynamic compression plate (DCP) over superior aspect of clavicle without damage to underlying neurovascular structures after open reduction of fracture. Limb was immobilized in a simple sling in patients. Rehabilitation was started immediately after plate fixation. Pendulum exercises were started initially followed by passive range of motion (ROM) for 2 weeks, followed by active assisted and full active ROM according to clinical and radiological signs of union of fracture. Usually, after 12–14 weeks, all patients returned to their original level of activity. Functional outcome was measured with constant score and DASH score while radiological assessment was done by radiologist. The fracture was considered as united when there was no tenderness at fracture site and X-ray showed bridging callus. Adverse event and complications were also noted. Patients were followed up at 2, 4, 6, 12, and 24 weeks after operation. Yes/no type of subjective questions pertaining to pain/complications, quality of life, and return to work, whether they would recommend surgery to someone else, were prepared for general satisfaction questionnaire outcome at the end of study. Depending on response, grading as poor, fair, good, very good, and excellent was done.

All statistical significances were established as $P < 0.05$. Two sampled *t*-test for gender, fracture type on functional outcome score, and side of fracture were done. Paired *t*-test was used for ROM of operated and normal shoulder.

SPSS software version 20.0 was used for statistical analysis.

RESULTS

Mean time for radiological union was 39.4 days (range 32–179 days) [Table 1].

Beyond 180 days, in the absence of clinical and radiological signs of union, one case was considered as non-union. After bone grafting, it also united. There were hardware prominence problems in 10 cases. Hypertrophic scar was seen in 2 cases. Superficial infection was seen in one case which resolved with oral antibiotics alone. Paresthesia in 2 cases also resolved in 10–12 weeks. Mean constant and DASH scores were 95.35 ± 6.26 (range 81–98) and 0.98 ± 2.19 (range 0–9.2), respectively. There were no other complications in our patients.

Overall, satisfaction rate was quite high (90.2%) [Table 2].

Thus, there was no gross restriction of movements of shoulder on affected side [Table 3].

DISCUSSION

Conservative management has been mainstay of management of middle third clavicle fractures irrespective of displacement or comminution in India. However, there are many cases of non-union (15%) in displaced clavicle fractures according to literature. Furthermore, there are other problems such as malunion, decreased ROM of shoulder, and lower satisfaction rate after conservative

Table 1: Demographic details

Variable	Number of patients (%)
Gender	
Male	33 (64.71)
Female	18 (35.29)
Side	
Dominant	27 (52.94)
Non-dominant	24 (47.06)
Robinson type	
2B1	34 (66.67)
2B2	17 (33.33)

Table 2: General satisfaction questionnaire outcome

General satisfaction	Number of patients <i>n</i> =51 (%)
Excellent	34 (66.67)
Very good	12 (23.53)
Good	3 (5.88)
Fair	2 (3.92)
Poor	2 (0)

Table 3: Range of motion

Range of motion in degrees	Affected side	Normal side
Mean abduction	174.09	175.95
Mean ext. rotation	83.64	85.127
Mean int. rotation	66.608	68.608
Mean flexion/extension	174.35	176.17

management (one-third not satisfied).^[7] According to literature, there is a significant reduction in malunion cases and non-union cases (only 2.2%) if operative treatment is performed.^[8] Hence, we evaluated results of operative treatment at our Medical College Hospital and compared it with literature studies.

In our study, demographic variables were comparable to other studies. In our study, mean time for radiological union was 39.4 days only with operative treatment. In study conducted by Naveen *et al.*, time for union in clavicle fractures treated conservatively was 11.29 weeks, i.e., 79.03 days.^[9]

In our study, only there was only one case of non-union of 51 patients were present (<2%). According to literature, there is risk of 15–20% that displaced clavicle fractures treated conservatively can go into non-union and about 2.2% if treated operatively.^[9] Thus, our results are consistent with literature. Overall, satisfaction rate after operative treatment was quite high in our study. This is consistent with literature.^[10] Mean constant and DASH scores were correlating with literature. Open reduction and internal fixation of clavicle can be performed with either plate or intramedullary pin fixation. However, since plate fixation can provide immediate rigid fixation, we performed plating over intramedullary pin fixation.^[11]

There were hardware problems in 10 cases of 51 patients, that is, about 19.60% of cases. These included screw loosening (4 cases) and hardware prominence in 6 cases (i.e., 11.76%). This can be explained by the fact that clavicle is subcutaneous bone, and there is less soft tissue envelope over implanted hardware contributing to hardware problems.^[12] To decrease hardware problems recently, there are studies which advocate positioning hardware along the anterior surface of clavicle as opposed to superior surface of clavicle.^[13] However, we placed plate along superior surface only as it was decided in study protocol already, and we did not want to divulge from our methods decided while we got ethical committee approval. In literature also rates for early removal of prominent hardware is around 8% and wound problems due to hardware are about 5%.^[13] Hypertrophic scar in 2 cases (3.92%) and infection in 1 case (1.96%) are also thus consistent with literature due to subcutaneous location of hardware. However, we

did not encounter any major complications such as neural or vascular damage, implant breakage, skin necrosis, deep infections, or adhesive capsulitis of shoulder in any case.^[13,14] ROM of shoulder was near normal in almost all patients who were operated with plating.

CONCLUSION

Open reduction and internal fixation of midshaft clavicle fractures give good functional and radiological outcomes with high patient satisfaction rate without any major complication. However, there was no control group in our study and follow-up period was short; hence, we cannot comment about late complications of procedure.

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Prevalence of Congenitally Missing Premolars in College of Dentistry, King Khalid University, Abha, Kingdom of Saudi Arabia: Can Early Treatment Make A Difference?

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Abstract

Introduction: Congenitally missing teeth are those teeth whose tooth germ did not develop adequately to allow the disparity of the dental tissues. Inherited absence of mandibular second premolars has an impact on orthodontic patients. The orthodontist should make the proper treatment plan regarding management of the edentulous space. The purpose of this study was to determine the prevalence of congenitally missing premolar in children aged 6–14 years who attended the College of Dentistry, King Khalid University, Abha KSA using OPGS.

Materials and Methods: In this retrospective study, a total of 1100 panoramic radiographs (OPG'S) of children who attended dental clinics at College of Dentistry, King Khalid University, Abha, were viewed for congenitally missing premolar with age group of 6–14 years. Digital orthopantomogram was examined in a standard manner under good lighting conditions. Data were collected and embarked into spreadsheet (Excel 2013: Microsoft office) and analyzed.

Results: A total of 1100 OPG'S were viewed for congenitally missing premolar with age group of 6–14 years. The prevalence for congenitally missing premolar was seen more in girls (59.4%) than boys (40.6%). The frequency of most congenitally missing premolar was mandibular 2nd premolar followed by maxillary 2nd premolar in both girls and boys.

Conclusion: Congenitally missing premolars were seen more in girls than boys, and mandibular 2nd premolar was most common missing tooth followed by maxillary 2nd premolar. Some early decisions that the orthodontist makes for a patient whose inherited mandibular second premolars are missing can influence the dental health for a lifetime. Therefore, the accurate decision must be made at the appropriate time.

Key words: Congenitally missing teeth, Hypodontia, Premolars

INTRODUCTION

The most frequent developmental and congenital dental anomaly is tooth agenesis. Congenitally missing teeth (CMT) refer to teeth whose germ did not develop adequately to allow the differentiation of the dental tissues.^[1] The most dental abnormalities in tooth shape, number, and position

usually lead to problems in maxillary and mandibular arch length and occlusion, which can have an influence on orthodontic treatment.^[2] CMT compose the most common developmental anomaly of the human dentition, mostly arising in about 25% of the population.^[3] Excluding third molars, the prevalence of tooth agenesis is approximately 4.3–7.8%. Among this, mandibular 2nd premolar is the most commonly missing teeth followed by maxillary lateral incisors and then maxillary 2nd premolar.^[3] The etiology is usually attributed to MUTATION of some genes (PAX9 AND MSX1), besides to some etiological events in the prenatal and postnatal periods.^[4] Epidemiological studies display less prevalence of agenesis in the black race when estimated with the white race, while Asians showed increased tooth agenesis compared to whites.^[5] On basis

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of sexual differences, the prevalence of tooth agenesis in women was more affected than men.^[5]

Congenitally absence of premolars affects many orthodontic patients. Early diagnosis of premolar agenesis is hindered by delayed calcification. By the age of 8 years, the dental follicle or germ should be visible on X-ray, but this may not be the case until around 11 years of age. Failure to detect an unerupted premolar may lead to unnecessary space loss, crowding, or collapse in the dental arch. Hence, it's the orthodontist who has to take the proper decision at the correct time regarding management of the edentulous space.^[6]

The purpose of this study was to determine the prevalence of congenitally missing premolar in children aged 6–14 years who attended the College of Dentistry, King Khalid University, Abha KSA using OPGS and yes, early treatment can make a difference.

MATERIALS AND METHODS

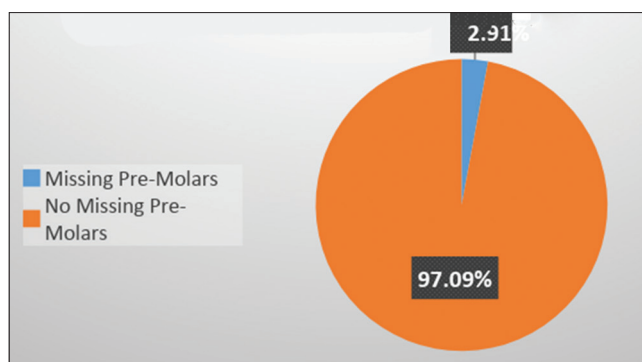
In this retrospective study, a total of 1100 panoramic radiographs (OPG'S) of children who attended dental clinics at COD, KKU, Abha were viewed for congenitally missing premolar with age group of 6–14 years. Digital orthopantomogram was examined in a standard manner under good lighting conditions, standard screen brightness, and resolution. A tooth was considered congenitally missing when the absence of crown mineralization was ruled out from the OPG'S. Data were collected and entered into spreadsheet (Excel 2013: Microsoft office) and analyzed.

RESULTS

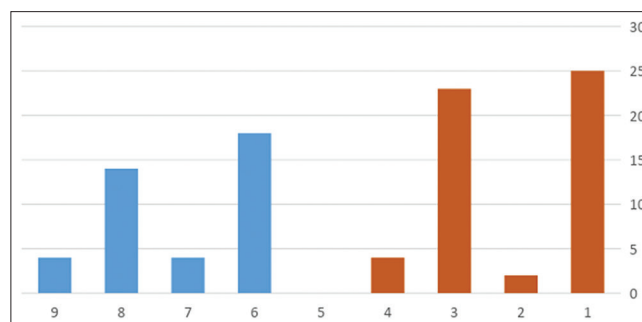
A total of 1100 OPG'S were viewed for congenitally missing premolar with age group of 6–14 years. Of these 32 (2.91%), OPG's had congenitally missing premolar as shown in Graph 1. Of these 19 were girls and 13 were boys. The prevalence for congenitally missing premolar was seen more in girls (59.4%) than boys (40.6%) as shown in Table 1. The occurrence of a total number of congenitally missing premolar was 94 in both the gender (Boys - 40 and Girls - 54). The frequency of most CMT was mandibular 2nd premolar followed by maxillary 2nd premolar in both girls and boys as shown in Table 2. Graph 2 also shows the occurrence of congenitally missing premolar by type and gender.

DISCUSSION

Developmental dental anomalies are frequently observed during routine dental examinations.^[7] When anomalies



Graph 1: Prevalence of missing pre-molars among the study subjects



Graph 2: Occurrence of missing pre-molars by type and gender

Table 1: Number of subjects with missing premolars by gender

Gender	Frequency (%)
Girls	19 (59.4)
Boys	13 (40.6)
Total	32 (100)

Table 2: Occurrence of missing pre-molars by type and gender

Gender	Tooth	Total	Frequency (%)
Girls	Lower 2 nd pre-molar	54	25 (46)
	Lower 1 st pre-molar		2 (4)
	Upper 2 nd pre-molar		23 (43)
	Upper 1 st pre-molar		4 (7)
Boys	Lower 2 nd pre-molar	40	18 (45)
	Lower 1 st pre-molar		4 (10)
	Upper 2 nd pre-molar		14 (35)
	Upper 1 st pre-molar		4 (10)
Total		94	

in tooth number, shape, and position are seen, it leads to problems in maxillary and mandibular arch length and occlusion, and thus has an effect on orthodontic treatment planning. The etiology of these conditions is mostly related to certain genes besides to etiological events occurring in the prenatal and postnatal periods.^[1] Early identification of a treatable anomaly is important in planning comprehensive management of the young child.

These anomalies develop before the eruption of the teeth and are often familial. However, since their effects may commence with the eruption of either or both primary and permanent dentitions and persist throughout life, some of the undesirable effects should be preventable. Functional, esthetic and occlusal disharmony may be recognized sufficiently early to demand interprofessional consultation and treatment in specific cases.^[7] CMT constitute the most common developmental anomaly of the human dentition, occurring in approximately 25% of the population.^[1]

In this retrospective study, a total of 1100 panoramic radiographs (OPG'S) of children who attended dental clinics at COD, KKU, Abha were viewed for congenitally missing premolar with age group of 6–14 years. Digital orthopantomogram was examined in a standard manner under good lighting conditions, standard screen brightness, and resolution. Of these 32 (2.91%), OPG's had congenitally missing premolar. Of these 19 were girls and 13 were boys. The prevalence for congenitally missing premolar was seen more in girls (59.4%) than boys (40.6%) as in Table 1. A total number of 94 congenitally missing premolar were seen (Boys - 40 and Girls -54). The frequency of most congenitally missing premolar was mandibular 2nd premolar followed by maxillary 2nd premolar in both girls and boys as shown in Table 2 and is similar to the results of many previous studies.

The orthodontist should decide properly regarding management of the edentulous space. These spaces can be closed or left open. If space will be left open for further restoration, for correct orthodontic treatment one should create the correct amount of space and to leave the alveolar ridge in an ideal condition for future restoration. If space will be closed, the clinician must avoid any disastrous adjustments to the occlusion and the facial profile. Some prior decisions that the orthodontist makes for a patient whose inherited mandibular second premolars are missing will affect his or her dental health for a lifetime. Therefore, the correct decision must be made at the appropriate time.^[6]

The clinical inference is must because the early diagnosis of a given dental anomaly can alert the clinician regarding the dental anomalies in the same patient or family, permitting early diagnosis, and timely orthodontic management.^[1] As in the present study, most frequently CMT were 2nd premolars, so early treatment can really make a difference by following Dr. Kennedy's general concept. Dr. Kennedy reported four main principles in managing missing second premolar cases: Establish the correct amount of space, preserve the occlusal table,

preserve the alveolar ridge set up treatment in such a way that the incisors will be in the correct positions at the end of treatment.^[8]

In prevalent terms, patients with minimal crowding, deep overbites, retrusive incisors, decreased lower facial height, and flat mandibular plane angles are typically best managed by nonextraction. In such cases, provided there is sufficient root support and absence of infraocclusion, retain the primary second molars for as long as possible. Patients with greater amounts of crowding molar or midline asymmetries, protrusive tendencies, minimal overbites or anterior open bites, and increased anterior facial height are frequently best managed with extractions and space closure. In such cases, one is likely to remove the retained primary molar. If you plan to retain the molar, look for the quality of occlusion and alveolar bone so as to have the best environment for the final restoration. If one wishes to close the edentulous space, be sure the incisors remain in good position to provide good facial balance.^[8]

CONCLUSION

Congenitally missing premolars were seen more in girls than boys, and mandibular 2nd premolar was most common missing tooth followed by maxillary 2nd premolar. Careful observation and appropriate investigations are required to diagnose the condition for proper treatment.^[9] Hence, early diagnosis and treatment of congenitally missing premolar can reduce the complications related with agenesis of the premolar. Early decisions that the orthodontist makes for a patient whose mandibular second premolars are congenitally missing will affect his or her dental health for a lifetime. Therefore, the correct decision must be made at the appropriate time.

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Effects of Oral Submucous Fibrosis on Auditory Tube Function: A Case-control Study

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Abstract

Background: Oral submucous fibrosis (OSMF) is a precancerous condition, recognized as collagen disease with resemblance to localized scleroderma. The study is to analyze the middle ear pressure of OSMF patients of various grades of disease.

Materials and Methods: A total of 40 OSMF patients (80 ears) and 40 healthy controls (80 ears) were analyzed for middle ear pressure by the use of impedance audiometry.

Results: The impedance audiometry test shows statistically significant difference in middle ear pressure of OSMF patients and control.

Conclusion: The study suggests that the middle ear pressure may be affected by disease and its progression.

Key words: Impedance audiometry, Middle ear pressure, Oral submucous fibrosis

INTRODUCTION

Oral submucous fibrosis (OSMF) is a chronic, insidious process characterized by juxtaepithelial deposition of fibrous tissue followed by fibroelastic changes of lamina propria with epithelial atrophy causing trismus and inability in total.^[1] The disease is having great resemblance to localized scleroderma. The disease is having great resemblance to localized scleroderma, although vesicle formation use to occur.

The most common cause is chewing areca nut,^[2] although other causes are chronic iron and Vitamin B-complex deficiency, autoimmunity, hypersensitivity, and genetic predisposition.

Histopathologically changes such as edema, infiltration of inflammatory cells, excessive deposition of fibroblast,^[3] and constricted blood vessels can be seen. Severe cases of

OSMF show degenerative changes in deeper tissue along with muscle fibers.^[4,5] Changes in these muscles which are attached to auditory tube and soft palate leads to change in middle ear pressure and causes hearing impairment.^[6]

Pathogenesis of disease is mainly by reduction of phagocytes of collagen by fibroblasts, increase secretion of growth factors and decreased the production of antifibrotic cytokines.^[2]

Shah *et al.*^[7] clinically evaluated auditory tube function with the help of pure tone audiometry and found significant impairment in OSMF patients.

OSMF patients complain of soreness of mouth, intolerance to chilies and spicy foods, burning sensation of mouth, ulceration of oral mucosa, and difficulty in protruding tongue and opening mouth.^[8] Loss of hearing is due to blockage of auditory tube.^[9]

MATERIALS AND METHODS

The study was conducted at BMMSH Ranchi, India, between January 2017 and December 2017 on 40 OSMF patients with no other oral lesions and 40 age and sex-matched healthy controls after taking permission from ethical clearance of the institutional ethical committee.

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On basis of history and clinical features such as soreness of mouth, intolerance to chillies and spicy food, burning sensation of mouth, ulceration of oral mucosa, palpable fibrous bands and decrease mouth openings, the diagnosis of OSMF was established.^[10]

Patients were divided under three groups on the basis of mouth opening which was calculated using metallic caliper and scale taking edges of upper and lower jaw central incisors as reference point (0–10 mm, 11–20 mm, and 21–30 mm).

Detailed ENT examination was done by myself to rule out any other factors affecting the hearing ability and middle ear pressure.

Impedance audiometry was done using Interacoustic AT235 equipment. Small probe was inserted in auditory canal which emits low frequency (226 Hz) and continuous change of positive and negative pressure was created by pump of instrument. The compliance was measured in the form of graph, obtained of three types among which Type A is normal and Type B and C are abnormal suggesting of disease in middle ear. Shift in compliance peaks showed that the middle ear pressure is maintained and compliance peaks with no shift showed poorly function of auditory tube.

RESULTS

Subject group comprised 32 males and 8 females aged between 18 and 56 years (mean age being 28) and control group comprised 30 males and 10 females aged between 21 and 47 years (mean age being 27) [Table 1].

Comparison between mouth opening and type of curves on the basis of impedance audiometry result shows in OSMF group of 80 ears auditory tube function test revealed no shift in compliance peaks in 42 (53%) ears with –200 daPa pressure changes after swallowing. On comparing both groups, the result of auditory tube function test was highly statistically significant $P = 0.000$ [Figure 1].

On comparing mouth opening and auditory tube dysfunction, on the basis of auditory tube function test, the result obtained was statistically significant [Table 2].

DISCUSSION

OSMF is a chronic, insidious disabling disease involving oral mucosa, oropharynx, and rarely larynx.^[11] Disease characterizes by burning sensation of mouth, blanching and stiffness of oral mucosa, trismus, loss of gustatory sensation, hypomobility of soft palate and tongue, and hearing loss due to blockage of auditory tube.^[12] It affects about 0.2–1.2% of Indian population^[13,14] having male predominance.^[15] Mainly affects in the second and third decades of life. In my study, similar findings were present which was accordance with the studies of Gupta *et al.*^[16] and Shah *et al.*^[6] In the present study, most of the patients were beetle nut chewers which were also a main etiological factor for the disease to happen.

The malignant transformation of the disease is 4–13% worldwide and 7.6% in Indian population.^[17,18] Several staging and grading system proposed by various researchers on clinical and histological features.^[19,20]

Clinically, staging is done on the basis of features such as burning sensation of mouth, ulcer formation, blanching of mucosa, limited mouth opening, restricted tongue protrusion, and extension of fibrous bands.^[21,22]

Histologically in early OSMF shows fine fibrils of collagen, hypertrophic fibroblast, dilated and congested blood vessel, and edema, loss of rete pegs, and infiltration of inflammatory cells.^[3]

Pathologically changes seen in mucosa, submucosa, muscles, and deeper tissue.^[4] Binnie and Cawson reported homogeneous collagenous subepithelial zone along with degeneration of muscle fibers.^[23]

Oliver *et al.* reported that dense collagen bundles were extended into underline striated muscles.^[24]

Rajendran *et al.* reported focal lysis and hypercontraction of myofibers and extensive fatty infiltration between muscle bundles in biopsy patients of OSMF.^[4]

Palatal and paratubal muscles in the form of levator veli palatini, tensor veli palatini, tensor tympani, and salpingopharyngeus which regulate the patency and

Table 1: Age and sex distribution of OSMF subjects and controls

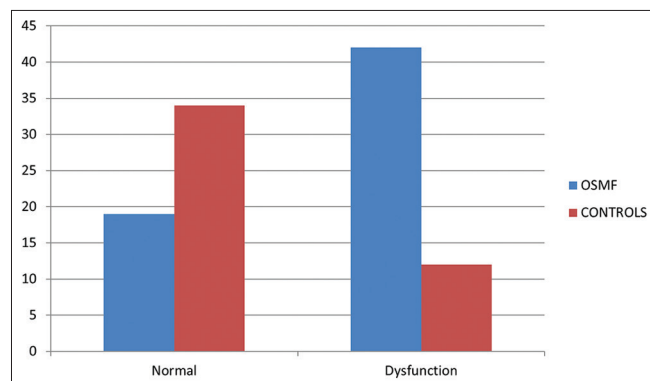
Age (in years)	Subjects			Controls		
	Male (n=32)	Females (n=8)	Total (n=40)	Male (n=30)	Females (n=10)	Total (n=40)
Range	18–56	28–47	18–56	21–47	25–37	21–47
Mean age	28	35	26	30	37	27

OSMF: Oral submucous fibrosis

Table 2: Result of comparison between Mouth opening and Auditory tube dysfunction

Mouth opening (in mm)	ETFT		P value
	Normal	Dysfunction	
0–10 (n=16)	0	16	P<0.05
11–20 (n=28)	12	16	
21–30 (n=36)	26	10	

ETFT: Eustachian Tube Function Test

**Figure 1: Result of Eustachian tube function test**

function of pharyngeal orifice resulting in impairment of function and patency of auditory tube, leading to hearing loss.^[9]

CONCLUSION

From this study, it is evident that the middle ear pressure got affected by disease process and cause hearing impairment. The result can be further justified by involving more sample size and patients of OSMF.

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A Clinical Study on Risk Factors for Recurrent Pulmonary Tuberculosis – a Hospital-Based Study

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Abstract

Aim of the Study: The aim of this study was to understand and identify risk factors in recurrent cases of pulmonary tuberculosis (TB).

Materials and Methods: A total of 54 patients attending tertiary teaching hospital with recurrent pulmonary TB were included in this study. Patients who were earlier cured using a four-drug treatment regimen of rifampicin, isoniazid, and pyrazinamide (RHZ) were included in this study. The risk factors studied were age, gender, race, duration of symptoms, lesion cavitation, extent of disease, diabetes mellitus (DM), alcoholism, HIV infection, delayed negative sputum conversion, treatment compliance, and medication doses. To detect recurrence, the patients were monitored for 7.7 ± 2.0 years after cure. Data were analyzed using the student's t-test and the Chi-square test.

Observations and Results: A total of 54 patients with symptoms of recurrence of pulmonary TB were included in this study. The mean age was 38.12 ± 4.60 years. There were 34 (62.96%) males and 21 (38.88%) females. The male-to-female ratio was 1.61:1. The mean age among the males was 40.09 ± 5.62 , and it was 34.12 ± 3.75 years. The mean duration of the symptoms was 82.45 ± 7.15 (12–238) days. There were 19 (35.18%) patients who were chronic alcoholics. The number of patients who showed cavity in their X-ray lung investigation was 46/54 (85.18%). The noncompliance among the diabetic patients was 2/54 (3.70%) with the total number of patients with DM was 20/54 (37.03%). Among the 54 patients, 31/54 (57.40%) patients were tested for HIV screening; among them, 07/31 (22.58%) tested positive for HIV. There were 07/31 (22.58%) positive HIV test patients in the recurrence group, and 09.01% HIV positive incidence in the nonrecurrence group which was statistically significant ($P < 0.05$).

Conclusions: Recurrence of TB was more common in HIV-positive patients, and in patients, who did not comply with the self-administered treatment (RHZ regimen). Patients presenting at least one of these risk factors can benefit from the implementation of a posttreatment surveillance system for early detection of recurrence. An alternative to prevent noncompliance with TB treatment would be the use of supervised treatment.

Key words: Isoniazid, Recurrence, Rifampicin, Risk factors, Tuberculosis

INTRODUCTION

An ideal antituberculosis (TB) treatments should provide high cure rates, few adverse effects, and low disease recurrence rates. The treatment protocols should be acceptable to the patients with minimal side effects. The three-drug regimen consisting of the combined use

of rifampin (RIF), isoniazid (INH), ethambutol, and pyrazinamide (PZA), meets the parameters as long as the medications are administered in the right doses and for the prescribed duration.^[1] The importance of the duration of the treatment protocol may not be appreciated by the naïve patients and there always tendency to stop the treatment with the improvement of symptoms initially. However, if the treatment protocols are followed strictly, the cure rates reach near to 100%, as well as rates of regimen change due to toxicity and rates of recurrence lower than 5%, can be obtained. Certain factors, such as duration of treatment, bactericidal/bacteriostatic activity of the medications, mode of administration (daily or intermittent), and noncompliance have been identified as being associated

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with recurrence of TB. With the outbreak of the HIV infection epidemic, some studies have shown higher recurrence rates in infected (HIV-positive) patients,^[2-8] whereas others show similar values.^[9-11] The treating physicians should always be aware of the risk factors for recurrence of pulmonary TB after achieving a cure, to take measures to ensure treatment success. In this context, a clinical study was conducted to observe and identify risk factors associated with the recurrence of cured pulmonary TB in patients treated with the short-course regimen used in Brazil (RIF+ INH+ ethambutol+ PZA regimen).

Period of Study

June 2015–May 2017.

Institution of Study

Kannur Medical College, Anjarakandy, Kannur, Kerala.

Type of Study

A retrospective, cross-sectional and controlled observational study.

MATERIALS AND METHODS

In the present study, 54 patients were included as per the inclusion criteria from among a total number of 3832 patients who were treated for pulmonary TB over 10 years. This required information was collected from the medical records department of the hospital. A total of 54 patients attending tertiary teaching hospital with recurrent pulmonary TB were included in the study. Patients who were earlier cured using a three-drug treatment regimen of Rifampicin, INH, Ethambutol, and PZA (RHZ) were included in the study. The risk factors studied were age, gender, race, duration of symptoms, lesion cavitation, extent of disease, diabetes mellitus (DM), alcoholism, HIV infection, delayed negative sputum conversion, treatment compliance, and medication doses. Institutional ethical clearance was obtained for the study.

Inclusion criteria

1. Patients aged above 20 years were included.
2. Patients of both genders were included.
3. Patients who were diagnosed as pulmonary TB and treated with four-drug regimen were included.
4. Patients with the risk factors such as mellitus, alcoholism, and HIV infection were included.
5. Patients with negative sputum conversion, treatment compliance, and medication doses were included in this study.

Exclusion criteria

1. Patients with age below 20 years were excluded.
2. Patients with three-drug regimen and other regimens were excluded from the study.

This was a controlled observational study comparing the incidence of recurrence in a group of individuals who had cured pulmonary TB and were exposed to a series of potential risk factors with the incidence of recurrence in another group of individuals who also had cured pulmonary TB but were not exposed to such risk factors. Initially, exposure was measured, and at a later time, it was determined whether or not recurrence had occurred. Therefore, we attempted to identify patient characteristics or attributes that could be associated with a greater likelihood of recurrence of pulmonary TB. The risk factors studied were age, gender, race, duration of symptoms, extent of disease, cavitation on chest X-ray, noncompliance, delayed negative sputum conversion (after the 4th month of treatment), DM, alcoholism, medication doses, and HIV infection. The treatment was self-administered, delivered to the patient every 30 days, and consisted of RIF+ INH + ethambutol+ PZA for 2 months and RIF+INH for another 4 months. Patients with HIV-positive screening and DM were administered additional RIF+INH for 7 months in the second phase of treatment. Patients with delayed negative sputum conversion received RIF+INH until they had three consecutive negative sputum samples. The dosage of medicines used in this study was adjusted according to the norms established by the Indian TB Association, i.e., weight < 45 kg, R: 300 mg, H: 200 mg, ethambutol 450 mg, and Z: 1000 mg; weight from 45 to 55 kg, R: 450 mg, H: 300 mg, ethambutol 600 mg, and Z: 1500 mg; and weight >55 kg, R: 600 mg, H: 400 mg, and Z: 2000 mg). The duration of symptoms was defined as the interval between the onset of the respiratory symptoms and the diagnosis of TB. Pulmonary lesions on chest X-rays were classified as “cavitary” or “noncavitary” and as “extensive” (affecting an area greater than that of one lung) or “nonextensive.” Treatment compliance was evaluated by pill counts, regularity in attending medical appointments, and information obtained from the patient or family members. All patients with a history of excessive alcohol consumption to the point of causing harm to their personal or professional relationships were considered alcoholics. All the data were analyzed using standard statistical methods.

OBSERVATIONS AND RESULTS

A total of 54 patients with symptoms of recurrence of pulmonary TB were included in this study. The mean age was 38.12 ± 4.60 years. There were 34 (62.96%) males and 21 (38.88%) females. The male-to-female ratio was 1.61: 1. The mean age among the males was 40.09 ± 5.62 , and it was 34.12 ± 3.75 years. The mean duration of the symptoms was 82.45 ± 7.15 (12–238) days. There were 19 (35.18%) patients who were chronic alcoholics. Among these only two patients (10.52%) accepted another

regimen of antituberculous treatment after diagnosed with recurrent TB. It showed that the rate of noncompliance was higher in alcoholics than in nonalcoholics ($P = 0.021$; where P significant at < 0.05). The number of patients who showed cavity in their X-ray lung investigation was 46/54 (85.18%). 11/54 (20.37%) patients declined again antituberculous treatment. The noncompliance among the diabetic patients was 2/54 (3.70%) with the total number of patients with DM was 20/54 (37.03%). Among the 54 patients, 31/54 (57.40%) patients were tested for HIV screening; among them 07/31 (22.58%) tested positive for HIV. The demographic and clinical features of patients who underwent HIV screening and those who did not undergo HIV screening were same. Delayed sputum conversion in the nonrecurrent group was 22.09% and in the recurrence group was 26/54 (48.14%). In all the 54 patients, the posttreatments follow-up after the initial pulmonary TB was 8.2 ± 3.18 years. An analysis of the demographic data and clinical findings on a multivariate basis, it was observed that there was no statistical difference in demographic data such as age, gender, extent of disease, cavitation in the lungs, delayed negative sputum conversion alcoholism, and DM between the patients who developed recurrence and those who did not [Table 1]. There was a statistical significant correlation between the two groups in regards with delayed sputum conversion, DM, and HIV screening positive result ($P < 0.05$), [Table 1].

There was also no difference regarding the doses of RIF, INH, ethambutol, and PZA between the two groups [Table 2]. The rates of treatment compliance or noncompliance (regular or irregular use of the medication) ($P = 0.018$) as well as of HIV-positivity and HIV-negativity ($P = 0.31$) were different between the two groups [Table 1]. There were 07/31 (22.58%) positive HIV test patients in the recurrence group and 09.01% HIV-positive incidence in the nonrecurrence group which was significant statistically ($P < 0.05$), [Table 1]. The overall recurrence was 54/3832 (%) in the present study. The number of patients developing recurrence within 12 months was 23/3832 (0.060%) and between 13 and 24 months was 16 (0.41%), and the remaining 15/3832 (0.39%) were between 25 and 96 months. In the HIV-positive patients, recurrence occurred within 14–49 months (mean of 18 months) after cure, whereas in the HIV-negative patients, recurrence occurred within 32–72 months (mean of 39 months; $P = 0.548$).

DISCUSSION

In the present study, 54 patients were included as per the inclusion criteria form among total number of 3832 patients who were treated for pulmonary TB over

Table 1: The demographic data and correlation between the patients who developed recurrence and without recurrence (n=54)

Observation	Recurrence group	Without recurrence	P
Mean age	38.12±4.60	39.21±6.11	0.612
Gender incidence ratio	1.61: 1	1.66:1	0.725
Extent of disease	Moderate-to-severe	Moderate-to-severe	Moderate-to-severe
Cavitation of lung	85.18%	86.02%	0.601
Alcoholism-19/54	35.18%	36.11%	0.120
irregularity in using medications	38/54-70.37%	49.16%	0.018
Noncompliance of treatment in alcoholics	17/54-31.48%	-	-
Delayed sputum conversion	26/54-48.14%	22.09%	0.044
DM	37.03%	21.54%	0.027
HIV positive	22.58	09.01%	0.031

DM: Diabetes mellitus

Table 2: The treatment doses of patients with recurrence and without recurrence (n=54)

Anti-TB drugs	Recurrence group	No recurrence group	P
Rifampicin	10.3±2.8	10.5±3.57	0.435
INH	6.4±1.5	6.9±1.99	0.610
Ethambutol	18.76±2.7	17.35±6.30	0.723
PZA	28.76±3.5	27.11±7.23	0.813

TB: Tuberculosis, INH: Isoniazid, PZA: Pyrazinamide

10 years. These 54 patients were evaluated in terms of TB symptoms, alcoholism, and DM, as well as being submitted to sputum smear microscopy and chest X-ray. Throughout the treatment period, the patients were monitored monthly using the clinical evolution and sputum tests. Recurrence of TB is defined as a new episode of the disease after the cure of a previous episode. It can occur due to endogenous reactivation or to exogenous reinfection,^[12] which are conditions that are clinically indistinguishable^[13] but can be differentiated by molecular techniques.^[12-14] The molecular techniques are not available at community level health in India, and due to its cost-effectiveness are not used. However, the failure to use these techniques does not cause greater harm to patients since at recurrence; patients again receive the RIF+ INH+ ethambutol+ PZA regimen, which is indicated in cases of endogenous reactivation as well as in cases of reinfection. Review of epidemiological studies shows that in areas of low TB incidence, recurrence is usually due to endogenous reactivation.^[15] In areas of high incidence, the incidence of cases of recurrence attributed to reinfection can reach 75%.^[12] Recurrence due to reinfection is a constant risk over time;^[13] whereas recurrence due to reactivation seems to occur closer to the time of cure.^[16] The overall recurrence was 54/3832 (%) in the present study. The number of patients developing recurrence within 12 months was 23/3832 (0.060%) and between 13 and 24 months was 16 (0.41%) and the remaining

15/3832 (0.39%) were between 25 and 96 months. In the HIV-positive patients, recurrence occurred within 14–49 months (mean of 18 months) after cure, whereas in the HIV-negative patients, recurrence occurred within 32–72 months (mean of 39 months; $P = 0.548$). The recurrences occurring within 12 months in this study may be more likely due to endogenous reactivation. The remaining cases occurred during the observation period (an average of two cases per year), and it was not possible to infer whether they were due to reactivation or to reinfection. Incomplete bacteriological cure, which is usually caused by irregular medication intake, is the most common cause of endogenous reactivation. Endogenous reactivation can also result from the use of regimens with low bactericidal potency, from inadequate treatment duration, from underdosing of the medications or from the inappropriate choice of medications, and ignoring the presence of preexisting resistance.^[4,6,7,13,17,18] In the present study, the regimen used was appropriate in terms of its composition, duration, and indication (treatment-naïve patients living in an area of low prevalence of primary resistance), and doses prescribed. Doses of INH higher than the 5 mg/kg of body weight recommended for adults were used due to the formulation of the capsule (300 mg of RIF and 200 mg of INH), which does not allow the prescription of the ideal INH dose without lowering the RIF dose.^[19] In the present study, only noncompliance and HIV infection proved to be related to higher rates of recurrence. Unlike previous studies, which have demonstrated that recurrence is more frequent in patients with DM, in those with extensive disease, and in those with pulmonary cavitation at the beginning of the treatment, the present study did not confirm that these conditions are risk factors for recurrence. Regarding DM, it is possible that the results of the present study are mainly due to the greater treatment compliance. Alcoholism has been identified as a major predictor of noncompliance from the initiation of TB chemotherapy, being a common cause of abandonment, death, and recurrence of TB.^[20] In recent studies, poor treatment compliance has been a significant risk factor for recurrence of TB in HIV-positive patients.^[6,21] In the present study, alcoholism was more common in patients who did not comply with the treatment than in those who did. However, alcohol abuse, in its relationship with recurrence, is no longer important when noncompliance is considered, since it is not alcoholism that leads to recurrence of TB, but rather treatment noncompliance. A limitation of many of the studies is the lack of information about the degree of immunosuppressant effect of HIV-positive patients, since severity of immunosuppression is a predictor of TB recurrence.^[21,22] In one of those studies, recurrence in HIV-positive patients only occurred in individuals with HIV-related symptoms, which are indicative of a more

advanced stage of immunosuppression.^[5] In other studies, low CD4 counts proved to be associated with a greater likelihood of recurrence.^[21,24] In addition to the limitation imposed by the small number of HIV-positive patients in the present study, this topic was also not investigated. Since AIDS treatment was little effective at the time, the patients were recruited, it is to be presumed that the immunity of many patients was compromised. The results of the present study indicate that noncompliance and HIV infection are independent risk factors for recurrence of TB after cure using the self-administered RIF+ INH+ ethambutol+ PZA regimen.

CONCLUSIONS

The patients cured of TB who present at least one of these risk factors can benefit from the implementation of a posttreatment surveillance system for early detection of possible cases of recurrence. To prevent noncompliance with TB treatment, especially in areas of high prevalence of TB and HIV infection, it becomes more important that supervised treatment be used. For HIV-positive patients, the use of INH after TB is cured can be contemplated. However, clinical and epidemiological studies are needed to calculate the cost-benefit ratio of this chemoprophylaxis, as well as to determine the appropriate duration of treatment.

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Hernia of Morgagni in Adults: Atypical Presentations

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Abstract

Background: Foramen of Morgagni hernias is rare diaphragmatic hernias, usually occurring on the right side and located in the anterior mediastinum because of the retrosternal location of the foramen of Morgagni. Adult patients diagnosed with a foramen of Morgagni hernia are usually asymptomatic. Although most remain asymptomatic, some patients develop symptoms of dyspnea, cough, sternal pain, and bowel obstruction depending on the extent of the hernia. The hernia usually contains omentum, bowel (colon), and sometimes liver.

Materials and Methods: We present three adult patients one presenting with dyspnea, the second presenting with acute intestinal obstruction, and the third patient was diagnosed to have the hernia on routine investigations.

Conclusion: Clinical awareness of atypical presentations and diagnostic difficulties might help in prompt diagnosis and early surgical treatment of this otherwise potentially fatal disease.

Key words: Atypical presentation, Hernia of Morgagni, Prompt surgery

INTRODUCTION

Hernia of Morgagni results from a defect in anterior diaphragm.^[1] It is a rare variety of diaphragmatic hernia and less frequently seen when compared to Bochdalek hernia which occurs because of posterior defect in the diaphragm.^[2] Usually, abdominal contents herniate into the thoracic cavity, stomach, and intestine being the common contents. This hernia is mostly asymptomatic^[3] and is usually detected incidentally on routine evaluation with chest X-ray done for other reasons. However, a smaller subset of patients present with symptomatic hernia. The symptoms in such patients are those of intestinal obstruction and consequent bowel ischemia or dyspnea. A high index of suspicion is required to diagnose such hernia whenever patients present with such symptoms.^[4] A missed diagnosis would lead to significant morbidity and

considerable mortality. The diagnosis is usually confirmed by a lateral chest radiograph, barium studies, or computed tomography of the chest with contrast.

The hernia of Morgagni can be approached through abdomen or thorax and can be done using laparoscopy also.^[5] The mesh repair is indicated whenever defect is large.

MATERIALS AND METHODS

In our hospital, we retrospectively studied three cases of hernia of Morgagni their presentations and outcome of treatment. A 44-year-old female patient with a history of respiratory difficulty and epigastric pain was referred to the department of surgery. Respiratory sounds were found to be diminished at the right basal region on auscultation. Posteroanterior chest X-ray, a homogeneous increase in opacity at the right paracardiac area was observed. This opacity was located anteriorly on lateral chest X-ray. Computerized tomography revealed bowel loops (transverse colon) in the right paracardiac area. Elective surgical repair of Morgagni hernia through transabdominal route under general anesthesia was planned. Abdomen was opened by upper midline vertical incision and on opening,

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the abdomen transverse colon and omentum were seen entering the diaphragmatic defect on the right side in the retrosternal area. After reducing the contents (colon and omentum) back to abdomen an oval defect of size 4 cm × 3 cm was found in the anterior part of diaphragm on the right side in the retrosternal area (space of Morgagni or space of Larrey) [Figures 1 and 2]. The hernia defect was repaired by non-absorbable suture (No 1 prolene) in interrupted fashion. The patient had uneventful post-operative period and was discharged after 6 days.

The second patient was an 86-year-old elderly lady who presented with features of intestinal obstruction of 2 days duration Figure 3. Chest X-ray revealed bowel loop with air-fluid level in the right lower chest. Computed tomography abdomen was suggestive of bowel loops (transverse colon) herniating through the diaphragm. As trial of conservative management failed, she was taken up for surgery. Laparotomy, reduction of hernia contents (transverse colon and omentum) and closure of the diaphragmatic defect with mesh was done. The lady was on ventilator support for 24 h which was gradually weaned off. Unfortunately, she developed pulmonary pneumonia and expired due to respiratory complications on post-operative day 14 after making a brief recovery.

The third patient was a 30-year-old male who was referred to surgical department for an abnormal finding in a routine chest X-ray. We further investigated the patient with a CT thorax which confirmed the diagnosis as to be hernia of Morgagni with transverse colon as its content [Figure 4]. After discussing with the patient, he was subjected to laparoscopic repair where the transverse colon was found to be herniating into the defect of about 3 cm × 3 cm in the anterior aspect of diaphragm. The defect was repaired with composite mesh. The post-operative period was uneventful and the patient was discharged from the hospital on post-operative day 4 and is doing well after 6-month post-surgery.

DISCUSSION

The retrosternal diaphragmatic hernia described by Morgagni in 1769 makes up <2% of reported diaphragmatic defects.^[6] The hernia occurs between the xiphoid process of the sternum and costochondral attachments of the diaphragm where the internal mammary vessels pass through the diaphragm to become the epigastric vessels. It results from a failure of muscle tissue to spread over the area. This potential space is covered by pericardium on the left side, and so more hernias occur on the right. The hernia usually has a sac, unless the sac has ruptured in prenatal life. This rare hernia may be found in childhood but is more likely to be present in adults. The symptoms vary, and they may be only vague fullness and cramping

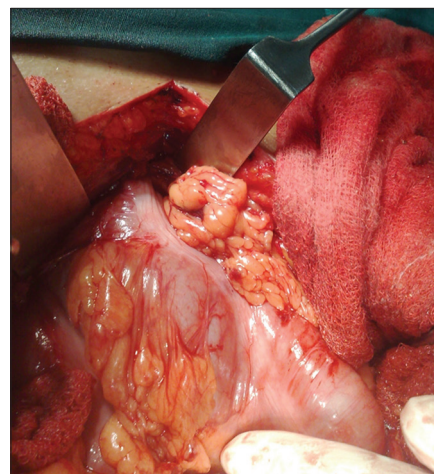


Figure 1: Transverse colon herniating into retrosternal defect

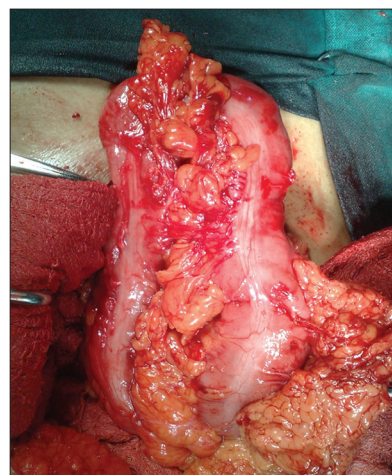


Figure 2: Contents of hernia (omentum and transverse colon) reduced



Figure 3: Erect abdominal and chest radiograph showing air-fluid level in the right hemithorax

to obstructive in nature, some patients may present with respiratory difficulty/dyspnea. There seems to be a larger percentage of female patients, and obese patients are

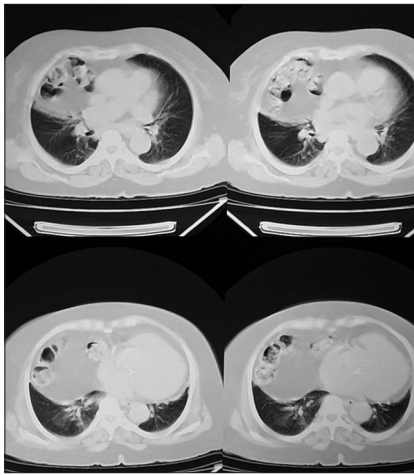


Figure 4: Contrast-enhanced computed tomography thorax showing omentum and transverse colon in the right hemithorax

more symptomatic.^[7] The hernia frequently presents as an incidental abnormal finding on chest X-ray films. The film may show a mass or even a fluid level. The viscera in the sac usually include one or more of the following: Colon, omentum, stomach, and small bowel. An upper gastrointestinal series or barium enema can characterize abdominal contents in the sac. Computed tomographic scanning is particularly useful and has a reported 100% sensitivity for diagnosis.^[8]

The need for surgery depends on presentation. Although the majority of these hernias are asymptomatic, repair is recommended to avoid future complications. Operation is indicated when the colon is in the sac, as there is a high risk of obstruction. If the hernia is small or if it contains omentum only, operation is indicated when symptoms are recurrent and bothersome. Treatment options include transabdominal, transthoracic and laparoscopic repair, and mesh repair are done when the defect is large.^[9,10]

CONCLUSION

Morgagni hernia constitutes 1–3% of congenital diaphragmatic hernias and usually presents later in adult life. The hernia is usually asymptomatic and may be detected incidentally on routine chest X-ray or the patient may present with symptoms of epigastric discomfort, dyspnea, and bowel obstruction. Repair is advised whenever bowel (colon) is the content of hernia because there is risk of obstruction and strangulation. Awareness of clinical entity of Morgagni hernia and its atypical presentation in adults would help in prompt diagnosis and early surgical management.

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Retrospective Study of Surgical Site Infection in an Urban Centre of Eastern India

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Abstract

Background: In compromised operation room and ward environment does extended prophylactic antibiotic for beyond 24 h do better for preventing surgical site infection (SSI)?

Materials and Methods: In this retrospective transverse cross-sectional study 899 (major = 699 and minor = 230) post-operated patients are investigated for the incidence of infection. The patient population is distributed in trauma, arthroplasties, and others as 508, 106, and 285, respectively.

Results: In major procedures infection developed as superficial incisional, deep incisional, and deep organ space are 4.33%, 1.20%, and 1.05%, respectively, and average total being 6.93%. In minor procedure, the values are 2.17%, 0.43%, and 2.70%. The incidence of SSI in arthroplasties was 11 (10.38%). Minimum period for identification for SSI 6 days in 11 cases and as late as 53 days in 1 case. Organism prevalence was *Staphylococcus aureus* 51.92% (MRSA = 51.85%), *Staphylococcus epidermidis* in 8, *Streptococcus* in 12, *Escherichia coli* in 2, *Klebsiella* in 1, and *Pseudomonas* in 2 cases. Combining debridement and suitable antibiotics SSIs controlled in 27 cases and failed in 25 cases.

Conclusion: Prolonged prophylactic antibiotic use cannot reduce the incidence of SSI. It makes delay in identification of SSI leading to difficulties in controlling it. Prophylactic antibiotic is never an alternative for the antiseptic surgical protocol.

Key words: Arthroplasty, Orthopedic operation, Prophylactic antibiotic, Surgical site infection

INTRODUCTION

Surgical site infection (SSI) is a major problem in clean non-contaminated orthopedic operations. Reasons, as defined in literature, are compromised operation room (OR) environment including inadequate sterilization, unrestricted entry of people,^[1] improper hand washing,^[2] and gowning^[3] ward environment^[4] and hygienic sense of patients and accompanying persons,^[5,6] compromised immunological status of patients, obesity^[7] and smoking, and lack of

appropriate prophylactic antibiotic administration.^[8] Prolonged pre-operative hospital stay is a potential cause of SSI.^[9] Many orthopedic surgeons believe that in a compromised situation where OR and ward environment are not up to the expected level the standard prophylactic antibiotic therapy may not be adequate and use to use more extended period of prophylactic antibiotic therapy for more than 5 days postoperatively. We conducted this retrospective study in a new rural Medical College in Eastern India, which is overcrowded and where 5 days post-operative prophylactic antibiotic was used, to determine the overall rate of SSI.

MATERIALS AND METHODS

It is a retrospective transverse cross-sectional study of patient undergone clean orthopedic operations from January 1, 2012, to December 31, 2015, in Murshidabad

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Medical College excluding open injuries, definite immune-compromised state, and infections. Ethical committee approval is obtained duly. Study tools are in-patient hospital records.

899 patients (male = 642 and female = 257) of age ranging from 2 years to 87 years are included in this study. Pediatric (0–18 years) and adults (≥ 19 years) patients were 285 and 614, respectively. Included major and minor surgeries were 669 and 230 [Table 1]. Invasive surgical procedures that penetrate and expose a body cavity or have the potential for permanent anatomic or physiologic impairment or need extensive tissue dissection or transection are major surgery whereas minor surgery neither penetrates a body cavity nor causes permanent impairment of any bodily functions. Needle biopsies are included in minor surgery category. 420 major operations were done for various traumas at different body parts and that for arthroplasty in 106 cases. Major operation was done other causes were 143 which include tumor, deformity correction, osteonecrosis, arthrodesis of ankle, congenital deformities, entrapment syndromes, non-unions, and few others [Table 2]. Total of arthroplasties were 106 (hip = 93, knee = 8, shoulder = 2, and below = 3). Prophylactic antibiotics used were cefuroxime (1.5 g) in 212 and ceftriaxone (1 g) in 687 cases within 15–60 min before incision intravenously. Per-operative a second dose was administered in 97 cases. They were continued for 3 days

Table 1: Distribution of patients according to major and minor procedures and their age groups

Category of surgery	Age (2–18)	Age (19–87)	Total
Major	147	522	669
Minor	138	92	230
Total	285	614	899

Table 2: Regional and etiological distribution of major and minor procedures

Region	Numbers							
	Trauma		Arthroplasty		Others		Total	
	Major	Minor	Major	Minor	Major	Minor	Major	Minor
Foot and ankle	20	4	-	-	11	61	31	65
Leg	44	6	-	-	6	13	50	19
Knee	22	2	8	-	6	21	36	23
Thigh	68	14	-	-	19	4	87	18
Hip	58	12	93	-	31	12	182	24
Pelvis	7	-	-	-	2	2	9	2
Spine	9	-	-	-	2	-	11	-
Shoulder	40	-	2	-	2	5	44	5
Arm	21	2	-	-	6	8	27	10
Elbow	66	34	3	-	18	10	87	44
Forearm and wrist	61	6	-	-	31	3	92	9
Hand	4	8	-	-	9	3	13	11
Total	420	88	106	-	143	142	669	230

in 411 and 5 days in 488 cases. In infected cases, the first debridement was done as early as 6th post-operative day (11 cases) and as late as 53rd post-operative day (3 cases). Rest of the cases were debrided in between. Second debridement was done in 10 cases.

RESULTS

Infection developed in 46 (6.93%) cases in major procedure group where superficial incisional, deep incisional, and deep infection were 29 (4.33%), 8 (1.20%), and 7 (1.05%), respectively. The infection in minor procedure group was 6 (2.70%) which include superficial incisional infection in 5 (2.17%) and deep incisional infection in 1 (0.43%) cases, and none had Organ/space infection [Table 3]. Thus, the total average infections were 52 (5.78%) of 899 cases. Of the 106 cases of arthroplasties, 11 had an infection which includes 10 infections of 93 hip arthroplasties (superficial incisional = 5, deep incisional = 3, and deep = 2) and one infections of 8 knee arthroplasties. None of the other arthroplasties (shoulder = 2 and elbow = 3) had infection [Table 4]. After surgical management infection was controlled in 27 (51.92%) cases and in 25 (48.08%) cases including 5 arthroplasties implants were sacrificed. The most infecting microbes were *Staphylococcus aureus* 51.92% (MRSA = 51.85%). Other microbes were *Staphylococcus epidermidis* in 8, *Streptococcus* in 12, *Escherichia coli* in 2, *Klebsiella* in 1, and *Pseudomonas* in 2 cases [Table 5].

DISCUSSION

In the present series, the overall SSI rate in orthopedic major procedure is 6.93% and that of arthroplasty cases are 10.38%. Edwards *et al.* reported that the SSI after arthroplasties of hip and knee is around 2%.^[10] Possible reasons for this significantly higher SSI are (a) third-generation cephalosporin is used in almost half of the cases, (b) bacterial biofilm production on the interface implant and bone, (c) decolonizing mupirocin is used in none of the cases, (d) OR environment particularly number of person entry is compromised, (e) hygienic sense of most patients is below average, and (f) long pre-operative stay and overcrowding of patients in wards. In arthroplasty group, as it is a new medical college and arthroplasties are a new operation, restriction of unwanted person entry is further compromised.

Post SSI is recognized earliest on 6th and latest on 53rd post-operative day. This intervention is also delayed leading to poorer control of infection. This is because of continued antibiotic beyond 24 h which mask the clinical features of infection.

Table 3: Overall different types of infection and their percentage of major and minor groups

Type of surgery	Number of surgery	Infection			
		Superficial incisional	Deep incisional	Organ/space	Total
Major	669	29 (4.33)	8 (1.20)	7 (1.05)	46 (6.93)
Minor	230	5 (2.17)	1 (0.43)	-	6 (2.70)

Table 4: Number of different arthroplasties and their incidence of infection

Type of arthroplasties	Number of arthroplasties	Infection			
		Superficial incisional	Deep incisional	Organ/space	Total
Hip	93	5	3	2	10
Knee	8	1	-	-	1
Shoulder	2	-	-	-	-
Elbow	3	-	-	-	-
Total	106	6 (5.66)	3 (2.83)	2 (1.88)	11 (10.38)

Table 5: Prevalence of microbes in tissue collected during debridement in SSI cases and their sensitivity

Microbes	Number	MSSA	MRSA	Result	
				Controlled	Sacrificed
<i>Staphylococcus aureus</i>	27 (51.92)	13 (48.15)	14 (51.85)	11	16
<i>Staphylococcus epidermidis</i>	8 (15.38)			5	2
<i>Escherichia coli</i>	2 (3.85)			-	2
<i>Streptococcus</i>	12 (23.08)			10	3
Others	3 (5.77)			1	2
Total	52			27	25

noted the incidence of *S. aureus* and MRSA as 31% and MRSA as 49%. In the present series, incidence of *S. aureus* is 27 (51.92%) of which MRSA was 14 (51.85%). The higher incidence may be as a result of developing bacterial resistance due to a prolonged period of beta-lactam antibiotic therapy, non-use of decolonizing Mupirocin spray and higher prevalence of *S. aureus* in the hospital.

Bratzler *et al.*^[7] recommended as clinical guidelines that no prophylactic antibiotic is needed for clean orthopedic operations where no implant is inserted. However, it is supported by poor evidence. However, in any clean orthopedic operation with implantation and arthroplasties, single dose prophylactic first generation or second generation is adequate. In situations with beta-lactam hypersensitivity, clindamycin and aminoglycoside are to be considered. Perioperative dose repetition is dependent on duration of surgery or amount of blood loss. Decolonizing Mupirocin nasal or armpit spray is useful to prevent SSI by MRSA microbe. In the present study, these guidelines are not followed.

The limitation of this study is that it is a retrospective one. Hence, maintenance of stringent aseptic protocol cannot be ascertained completely.

CONCLUSION

Prolonged prophylactic antibiotic use cannot reduce the incidence of SSI. It makes delay in identification of SSI leading to difficulties in controlling it. Prophylactic antibiotic is never an alternative for the antiseptic surgical protocol.

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Relative Prevalence of Vitamin B12 and Folic Acid in Megaloblastic Anemia and Its Clinical – etiological Profile in a Tertiary Care Center

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Abstract

Background: Megaloblastic anemia (MA) causes substantial morbidity in patients with anemia and increasing number of MA is seen in clinical practice over the past 10–15 years.

Objectives: The objectives of the study were to study the relative prevalence of Vitamin B₁₂ and folic acid (FA) in MA and its clinical–etiological profile.

Methods: This is a cross-sectional observational study, conducted in the Department of Medicine, PGIMER and Dr. Ram Manohar Lohia Hospital, New Delhi, with patients of MA in whom detailed history; physical examination and nutritional assessment were recorded. Cobalamin and FA assays were done. Diagnosis of MA was confirmed by bone marrow aspiration and patients were further investigated to find out its cause.

Results: Majority of studied patients (46%) were in age group 22–40 years with male: female ratio of 2.6:1. Majority cases (95%) were from Hindu religion compared to Muslims (5%). The symptoms corresponding to anemia were the most common presentation of the patient. Fatigueness was present in 92%, exertional dyspnea and palpitation were the presenting complaints in 59% and 19% cases, respectively. Decrease appetite (80%), weight loss (54.6%), diarrhea (16%), mouth ulcer (14%), and paresthesias (11%) were the other common presenting symptoms. Pallor (96%) was most common finding in the study group. Skin hyperpigmentation was present in 48% and oral ulcer in 26% of patients. 54% of the participants had cobalamin deficiency, and 26% had FA deficiency, and 21% had both. 37% of cases had the nutritional background. Among non-nutritional etiology most frequently associated factors were alcohol and alcoholic liver disease (27%), and drugs (13%) followed by chronic infections and malabsorption.

Conclusion: The pathological conditions associated with the MA are much diverse. Proper diagnostic workup is essential before the use of hematinics and blood transfusion in all anemic patients.

Key words: Anemia, Megaloblastic anemia, Pancytopenia, Serum B12, Serum folic acid

INTRODUCTION

Megaloblastic anemia (MA) is a distinct type of anemia characterized by macrocytic red blood cells (RBCs) and

typical morphological changes in RBC precursors with the disparity in nuclear-cytoplasmic maturation. Basic underlying pathogenetic mechanism in MA is a deficiency of folic acid (FA) and/or Vitamin B₁₂ resulting in impairment of DNA synthesis.^[1]

However, pernicious anemia is a common cause of Vitamin B12 deficiency especially in persons of European or African descent, but dietary Vitamin B12 deficiency is a leading problem in the Indian subcontinent, Mexico, Central and South America, and selected areas in Africa.^[2,3]

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In India and other developing countries, most cases of MA are caused by a nutritional deficiency of FA, B12, or both. Pregnancy and lactation, alcohol, medications, infections, pernicious anemia due to intrinsic factor deficiency, and malabsorption are the other emerging causes for MA.^[2,4]

FA deficiency was reported to be more common than Vitamin B12 deficiency to cause MA in earlier studies; however, recent studies from India and other countries have shown Vitamin B12 deficiency is more common cause of MA than FA deficiency.^[5,6]

In this study, our aim is to study the relative prevalence of Vitamin B₁₂ and FA in MA and its clinical–etiologic profile.

MATERIALS AND METHODS

This study was conducted at the Departments of Medicine, PGIMER and Dr. Ram Manohar Lohia Hospital, New Delhi. This study was conducted on 97 enrolled patients who attended the medical clinics and medical ward.

Design of Study

This is a cross-sectional study.

Inclusion Criteria

The following criteria were included in this study:

- Hemoglobin (Hb) <10 g/dL in female and Hb <12 g/dL in male with pancytopenia (neutropenia and thrombocytopenia defined as absolute neutrophil count <1500 per mm³ and platelet count <150,000 mm³).
- Peripheral smear showing a megaloblastic picture (anisopoikilocytosis, macrocytosis, hypersegmented neutrophils, macrocytes, and presence of nucleated red cells).
- Bone marrow aspiration examination suggesting megaloblastic reactions.

Exclusion Criteria

The following criteria were excluded from the study:

- Age <14 years
- Previously diagnosed and on treatment (taking vitamin tabs/blood transfusion)
- Congenital disorders
- Pregnancy in 3rd trimester.

Following inclusion, diagnosis of the MA was established by bone marrow aspiration study. A detailed history including marital status, past or current comorbidities, and alcohol intake, depression, clinical and nutritional assessment was recorded on predesigned pro forma. A clinical examination and the laboratory profile of the subjects were also recorded. Nutritional Assessment was

assessed by Mini Nutritional Assessment-Short Form (MNA[®] -SF) questionnaire. The MNA[®] -SF screening maximum score is 14. Scores ≥12 indicate satisfactory nutritional status. A MNA[®] screening score ≤11 suggests malnutrition.

Hematological Assessment

All the subjects were undergone the following investigations:

- Complete hemogram
- Peripheral smear
- Red cells indices.

Biochemical Parameters

Following parameters were investigated further:

- Liver function test
- Serum cholesterol
- Serum triglyceride
- Serum lactate dehydrogenase
- Serum cobalamin level
- Serum FA level
- Serum iron level
- Serum ferritin level
- Thyroid profile (if needed)
- Bone marrow aspiration.

Imagings

To find out the causative factors responsible for MA, following test was performed when needed.

- Ultrasound abdomen
- Upper gastrointestinal endoscopy with/without biopsy
- Contrast enhanced computed tomography abdomen
- Colonoscopy with/without biopsy.

Statistical Analysis

The data so collected were analyzed using SPSS version 19[®] SPSS Inc. Mann–Whitney *U*-test and *t*-test were used to compare the mean of continuous variables depending on sample size, and Chi-square was used for nonparametric tests.

OBSERVATION AND RESULTS

Our study comprises a total of 97 patients including 70 male and 27 female cases. The age of patients studied ranged from 15 to 95 years with mean age of 39.06 ± 8.9 years. Majority of studied patients (46%) were in age group 22–40 years while the age groups 41–50 years and 51–60 years had 13 subjects (11%) each. All age groups had more number of male patients than the female counterparts except age group “age <21 years” which had comparatively more female cases [Table 1]. Majority cases of studied population (95%) were from Hindu religion compared to Muslims (5%).

Dietary preference of study group is shown in Figure 1. Majority of population 63% (61) were non-vegetarian while 37% (36) were vegetarians. Among vegetarians, vegans (18/36) were major group followed by lacto-vegetarians (10/36) and lacto-ovo vegetarians (8/36).

The symptoms corresponding to anemia (i.e. fatigueness, exertional dyspnea, and palpitation) were the most common presentation of the patient. Fatigueness was present in 92% of the study population; exertional dyspnea and palpitation were the presenting complain in 59% and 19% cases, respectively. Decrease appetite (80%), weight loss (54.6%), nausea and vomiting (22%), diarrhea (16%), mouth ulcer (14%), and parenthesis (11%) were the other common presenting symptoms [Table 2].

Clinical findings observed in participants are tabulated in Figure 2. Pallor was most common finding in the study group and present in 96% patient. Skin hyperpigmentation was present in 48% and oral ulcer in 26% of patients. Fever was the presenting clinical finding in 34% patient. Other common clinical signs in the study were pedal edema (25%), icterus (16%), and lymphadenopathy (8%).

In this study, the majority of patients (53%) had Hb level between 6 and 10 g/dL and 36% patients had Hb <6 g/dL.

Table 1: Composite age – sex distribution

Age group (year)	Sex		Total
	Female	Male	
<21	8	10	18
22–30	6	16	22
31–40	5	17	22
41–50	3	8	11
51–60	2	9	11
>60	3	10	13
Total (%)	27 (27.8)	70 (72.2)	97

Table 2: Presenting symptoms among the study group

Symptoms	Frequency
Fatigueness	89 (92)
Exertional dyspnea	57 (59)
Palpitation	18 (18.5)
Decrease appetite	78 (80)
Vomiting	21 (21.6)
Constipation	4 (4.1)
Diarrhea	15 (15.4)
Mouth ulcer	13 (13.4)
Weight loss	53 (54.6)
Paresthesias	10 (10.2)
Poor gait	10 (10.2)
Memory loss	2 (2)
Psychiatric symptoms	2 (2)

Mean Hb level of the study is 7.16 ± 2.41 with minimum and maximum value of 2.7 and 12.10 g/dL, respectively [Table 3].

Most of the patients (58%) had mean corpuscular volume (MCV) level more than 110 fL and 30% participants had MCV level between “95 and 110.” Only 11% of cases had MCV <95 fL [Figure 3].

Peripheral smear findings of all 97 participants are described in Figure 4. The most common findings were the presence of macrocytes (88%), anisocytosis (75%), and macroovalocytes (68%). Hypersegmented neutrophils were present in 43% patient. Other findings such as tear drop cells, Howell–Jolly bodies, polychromatocytes, nucleated RBCs, and target cells were also reported but were less frequent.

In our study, 52 (54%) of the participants had cobalamin deficiency, and 25 (26%) had FA deficiency, and 20 (21%) participant had patient had both cobalamin and FA deficiency.

Bone marrow examinations of the studied population showed cellular bone marrow with dyserythropoiesis and erythroid hyperplasia observed in 99%, 96%, and 96%

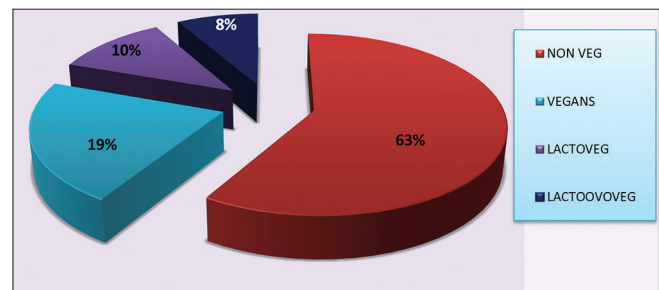


Figure 1: Dietary preference of study group

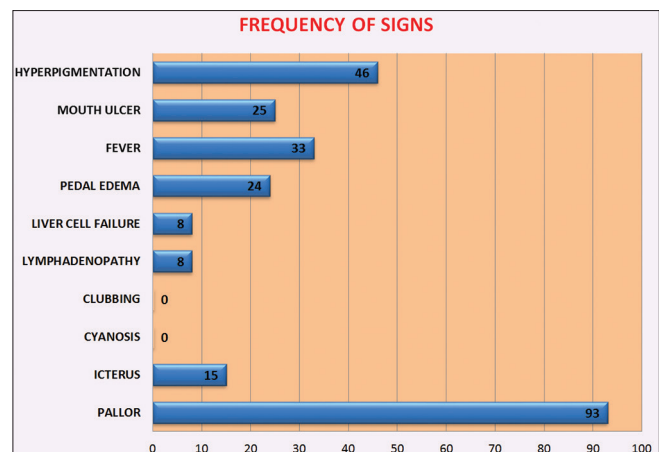


Figure 2: Clinical signs in the study group

cases, respectively. Pancytopenia was reported in 36% patient. Megaloblastic reaction was described in 78% cases while in 11% of cases bone marrow reaction was dimorphic. Bone marrow sample was inadequate in one case, and one case was diagnosed with acute lymphoblastic leukemia.

In the total number of 97 MA, 36 cases (37%) had nutritional background. Among non-nutritional etiology most frequently associated factors were alcohol and alcoholic liver disease (27%), and drugs (13%), and others factors are depicted in Table 4.

Table 5 elaborates the drugs associated with the MA in this study. Antiretroviral therapy (ART) was responsible for maximum cases in this category followed by metformin, pantoprazole, and antiepileptic drugs. One case of sulfasalazine used in ulcerative colitis also presented.

Moreover, the analysis shows that nutritional deficiency is entirely associated with vegetarian diet preference. Among vegetarian, it is vegans (18/36) who are affected most and followed by lacto-ovo vegetarian (10/36). There is no case

of nutritional deficiency among non-vegetarian and this distribution is statistically significant ($P < 0.0001$).

In nutritional group cobalamin deficiency was present in 31/36 cases and the combined deficiency was in 5/36 cases. In non-nutritional group 25/61 cases had isolated FA deficiency, 21/61 cases had cobalamin, and 15/61 cases had combined deficiency [Table 6].

DISCUSSION

MA causes substantial morbidity in patients with anemia. Data regarding the magnitude of the problem in different parts of India and the factors that might influence its incidence are lacking. Dietary deficiency of vitamin is well-established cause of MA. The pathological conditions associated with MA are much more diverse. In our study, investigations have revealed many causes of MA including nutritional deficiency, alcohol and alcoholic liver disease, drugs, HIV, tuberculosis, celiac disease, chronic pancreatitis, malaria, kalazar, tropical sprue, hypothyroidism, and hepatitis.

The study population comprised 97 patients, with age 39.06 ± 8.9 years (mean \pm standard deviation). The peak incidence of megaloblastic anemia was in the age group of 22–40 years (45.4%), followed by 19% in an age <21 years, and 14% in the age group more than 60 years.

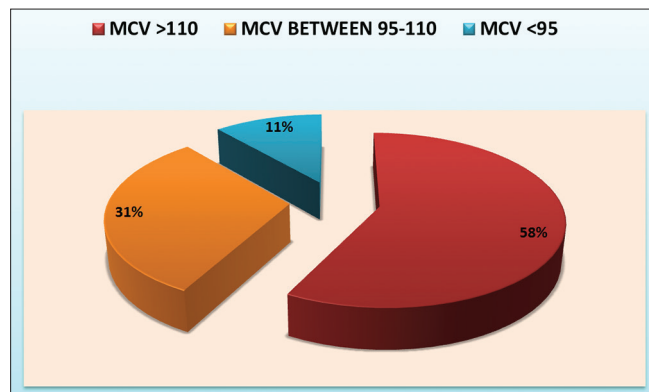


Figure 3: Stratifications of participants according to mcv level

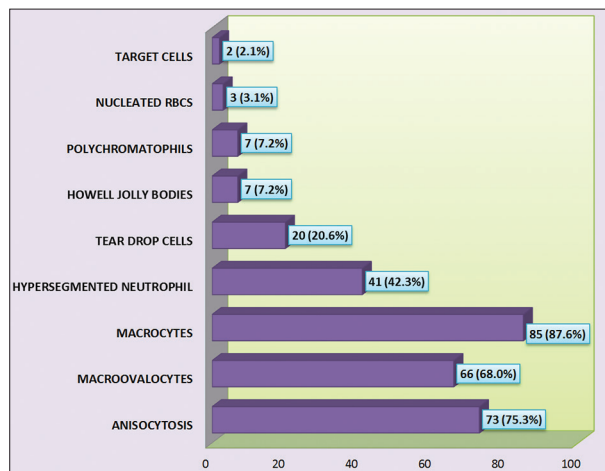


Figure 4: Findings on peripheral smears

Table 3: Stratifications of participants based on HB level

Hemoglobin level	Frequency (%)	Cumulative percentage
Low HB (6.0–10.0 g)	51 (52.6)	52.6
Very low HB (<6.0 g)	35 (36.1)	88.7
HB (>10.1 g)	11 (11.3)	100.0
Total	97 (100.0)	

Table 4: Etiological factors of megaloblastic anemia

Etiology	Frequency (%)	Cumulative percent
Nutritional	36 (37.1)	37.1
Alcohol and ALC. liver DS	25 (26.8)	63.9
Drugs	13 (12.4)	76.3
Tuberculosis	6 (5.2)	81.4
HIV	4 (4.1)	85.6
Celiac disease	3 (3.1)	88.7
Chronic pancreatitis	2 (2.1)	90.7
Kala azar	2 (2.1)	92.8
Malaria	2 (2.1)	94.8
ALL	1 (1.0)	95.9
Hepatitis B	1 (1.0)	96.9
Hypothyroidism	1 (1.0)	97.9
Tropical sprue	1 (1.0)	99.0
Total	97 (100.0)	

The peak incidence in the study by Khanduri *et al.* was seen in the age group of 10–30 years (48% of patients), and there was a preponderance of women (71%).^[7] Similar age distribution with a preponderance of younger patient is also observed by Unnikrishnan *et al.* from Pondicherry, India, in their study (mean 35.7 ± 16.1).^[8] Iqbal *et al.* from Pakistan studied MA and described similar age mean in their study.^[9] Mussarrat *et al.* observed, of 349 patients, 210 (60.17%) were males, and 139 (39.82%) were females in their study (male-female ratio - 1.5:1).^[10] Chandra *et al.* reported sex ratio of 1.33:1 in their study.^[11]

In the study, 95% participants belonged to Hindu community and only 5% patients were from Muslim community. Unnikrishnan *et al.* found 96% patient (25/26) of MA were from Hindu community and 4% (1/26) from Muslim.^[8]

Table 5: Drugs associated with MA

Drugs	Frequency (%)
ART (Virocom-N)	5 (5.2)
Metformin	2 (2.1)
Pantoprazole (40)	3 (2.1)
Epitoin (300)	2 (2.0)
Sulfasalazine	1 (1.0)
Total	13

Hindu Indians are usually strict vegetarian and are more prone to develop nutritional anemia. Matthews and Wood had studied the incidence of MA in Asians and found 95% patients from Hindu community and 5% from Muslim community, similar to our study.^[12]

In the study, nutritional MA was present in the only vegetarian group. 60% participants with cobalamin deficiency were vegetarians and 40% are non-vegetarian. In combined deficiency, 25% participants were vegetarian and 75% were non-vegetarian. In isolated FA deficiency group, all are non-vegetarian.

Britt *et al.* studied 25 Indian patients with MA and found 68% (17/25) participants were vegetarians. 96% of patients with cobalamin deficiency, 60% with combined deficiency, and 100% with FA deficiency were reported vegetarians.^[13]

Khanduri *et al.* described 87% of patients with cobalamin deficiency were vegetarian, and 71% of patients in combined deficiency were vegetarians.^[7] Chanarin *et al.* studied 138 Indian patients with MA in the year 1885 and their study all were vegetarians.^[14]

Clinical Profile

In our study, most frequent clinical symptoms associated with MA were fatigueness, decrease appetite, exertional

Table 6: Cobalamin and folic acid level among different etiology of MA

Etiological Factors	Serum cobalamin level			
	Low cobalamin		Normal cobalamin	
	Serum folate level		Serum folate level	
	Low folate	Normal folate L	Low folate	Normal folate
	Count	Count	Count	Count
Nutritional	5	31	0	0
Abd. Koch's	1	0	0	0
Alc. CLD	2	0	3	0
Alcoholic	4	0	16	0
ALL	1	0	0	0
ART induced	0	5	0	0
Chronic pancreatitis	1	1	0	0
Coeliac disease	0	0	3	0
Diss. Koch's	1	1	0	0
Hepatitis B	1	0	0	0
HIV	3	1	0	0
Hypothyroidism	0	1	0	0
Ileocecal TB	0	1	0	0
Kala azar Fever	0	2	0	0
Malaria	0	2	0	0
Metformin induced	0	1	1	0
Nutritional deficiency	5	31	0	0
Pantoprazole induced	0	3	0	0
Phenytoin induced	0	0	2	0
TB pericardial effusion	0	1	0	0
TBM	0	1	0	0
Tropical sprue	0	0	1	0
Sulfasalazine	1	0	0	0

dyspnea, weight loss, and vomiting in 92%, 80%, 59%, 55%, and 22% cases, respectively. Other symptoms such as palpitations were present in 19%, diarrhea in 16%, oral ulcers in 13%, and neuropsychiatric symptoms in 24% (paresthesias - 10%, poor gait - 2%, and memory loss - 2%), cases.

In a study by Khanduri *et al.* predominant symptoms were fatigue (70%), anorexia and gastritis (60%), fever (50%), and exertional dyspnea and palpitation (30%). They reported paresthesias, diarrhea, hyperpigmentation, and early graying of hair in <10% of patients.^[7]

Unnikrishnan *et al.* described all the patient (26) in their study, had symptoms of anemia (fatigue, dyspnea, and palpitation), 26% had bleeding manifestations, neurological symptoms in 26%, paresthesia in 17%, pedal edema in 26%, and diarrhea in 4% cases.^[8] Niazi and Khan reported the frequency of clinical features as pallor (90.25%), fever (56.73%), weakness (40.97%), bleeding manifestations (31.80%), and diarrhea (22.92%).^[15] Lindenbaum *et al.* found in their study that patients with cobalamin deficiency present with neuropsychiatric symptoms in 28% of cases, comparable to our result.^[16]

All the study has almost similar clinical presentations and its frequency. However, we did not find any patient with bleeding manifestation. This may be due to the absence of severe thrombocytopenia in our study.

In this study, observed clinical signs were pallor in 96%, knuckle hyperpigmentation in 47%, fever in 34%, oral ulcer in 26%, pedal edema in 25%, and icterus were present in 16% patients. Other signs such as lymphadenopathy and signs of liver cell failure were noted in 8.5% and 8%, respectively.

Unnikrishnan *et al.* reported pallor (100%), pedal edema (70%), hyperpigmentation (48%), neurological manifestation (26%), oral ulcer (43%), and icterus (26%) in their study.^[8]

Khanduri *et al.* described pallor (85%), glossitis (29%), mild icterus (25%), and hyperpigmentation of knuckles (18%) in their study.^[7]

Hematological Evaluation

In the hematological study, we found mean ESR of the patient were 29.03 ± 26.68 , and it was 19.63 in female and 21.48 in male. Mean hemoglobin value of study group was 7.16 ± 2.41 (female - 6.40 and male - 7.46). 88% of the participants had Hb level <10 g/dL, and 11% cases had value more than 10 g/dL, and 53% of the patients had <6 g/dL. Mean total leukocytes count (TLC) of the patient in this study was 7183.5 ± 5816.01 . 37% of the patients

had leukopenia, 32% of patients with normal TLC, and 28% of population were with leukocytosis in this study. Red cell indices and other analysis showed that the mean value of packed cell volume (PCV) was 20.5 ± 7.6 , mean value of mean corpuscular hemoglobin (MCH) was 38.04 ± 6.3 , mean MCHC was 34.9 ± 3.28 in this study. Mean MCV value in the study was 112.44 ± 13.27 (male - 111.53 and female - 114.83). In the study, 89% of patient had high MCV with 56% of patient had MCV >110. 11% of participants had MCV <95.

Mean value of platelet count was 1.56 ± 0.92 lacs/mm³. Thrombocytopenia was present in 50% of the patients. Mean value of reticulocyte count in the study was 2.27 ± 1.67 . In our study, 38% of the patient had high reticulocyte count. Studies showing similar hemogram analysis in MA are mentioned below.

Unnikrishnan *et al.* described mean of hematological parameters as Hb - 4.96 ± 1.26 , PCV - 14.65 ± 3.86 , reticulocyte count - 1.78 ± 0.48 , MCV - 111.8 ± 9.56 , MCH - 35.05 ± 4.43 , MCHC - 34.2 ± 2.35 , TLC - 4.30 ± 2.25 , platelet count - 0.98 ± 0.95 , and reticulocyte count - 2.5 ± 0.05 .^[8]

Niazi and Khan in their study, described hematological profile as 21.8% of patients had hemoglobin level of <5 g/dL, 65.3% of patients had hemoglobin level of 5–10 g/dL while 12.9% of patients had hemoglobin level of >10 g/dL (i.e. 87% of patients had Hb <10 g). 43.55% of patients had leukopenia while severe leukopenia was noted in 11.89% patients. Thrombocytopenia was detected in 72.20% patients.^[15]

Khanduri *et al.* in their study reported MCV ranged from 77 to 123 and reticulocyte count was found to be higher (more than 2) in 42% case.^[7] Chanarin *et al.* described 60% of patient had Hb <10, 84% of patients with raised MCV level.^[14]

Peripheral smear of the participants in our study showed macrocytosis in 88%, anisocytosis in 76%, and macro-ovalocytes in 68%, and hypersegmented neutrophil in 43%. Other cells present were Howell–Jolly bodies (7%), polychromatophils (7%), nucleated RBCs (3%), and target cells (2%) in small proportions.

Niazi and Khan found macrocytosis (68.5%), hypochromia (31.5%), anisopoikilocytosis (65.9%), and hypersegmentation of neutrophils (51.5%) on peripheral smear examination.^[15]

Unnikrishnan *et al.* in their study found that all the 26 patients with MA had hypersegmented neutrophils and/or macro-ovalocytes in peripheral smear.^[8]

Mwanda and Dave found anisocytosis, macro-ovalocytes in 83% cases, and hypersegmented neutrophils in 51% cases in peripheral smears.^[17]

Serum FA and Cobalamin Level

In our study, we found 53% (52/97) patients with isolated cobalamin deficiency and 26% (25/97) cases with isolated FA deficiency. Combined deficiency was present in 21% (20/97) patients. FA deficiency was present in 5/18 cases of vegans, but no any case in lacto-vegetarian and lacto-ovo vegetarian, and 40/61 cases of FA deficiency were present in non-vegetarians. Cobalamin deficiency was present in all vegetarian groups (36). 36/61 cases of cobalamin deficiency were present in non-vegetarians.

Khanduri *et al.* reported cobalamin deficiency in 65%, FA deficiency in 23%, and 12% cases of combined deficiency.^[7] Moreover, Unnikrishnan *et al.* reported cobalamin in 69% cases and FA deficiency in 19% cases in their study.^[8] Results of these studies regarding relative prevalence of cobalamin and FA deficiency are comparable to our result.

Chanarin *et al.* found 74% case with cobalamin deficiency and 26% case of FA deficiency but did not mention the combined deficiency.^[14]

Maktouf *et al.* found 98% patients with low serum cobalamin level and only 2% patient with FA deficiency. This large percentage of cobalamin deficiency and low of FA deficiency as comparison to our study may be due absence of group having combined deficiency.^[18]

Bone Marrow Aspiration Study

In BMA analysis, 99% smears showed cellular bone marrow. Dyserythropoiesis along with erythroid hyperplasia was noted in 96% cases. 80% of the BMA showed megaloblastic reaction and 18% dimorphic reaction. Pancytopenia was mentioned in 37% of cases. One case showed features of ALL. The incidence of pancytopenia was studied in 30.09% patients by Niazi and Khan.^[15] Moreover, Unnikrishnan *et al.* reported pancytopenia in 48% of case^[8] while Khanduri *et al.* found pancytopenia in 74/120 patients (62%).^[7]

Etiological Factors Responsible MA

In this study, most cases (37%) of MA were caused by nutritional deficiency (36/97).

Alcohol liver disease was the second most common cause of the MA accounting for 26% of cases (25/97). In this group alcohol as etiological factor was present in 20 cases and alcoholic liver disease was in 5 cases. Third most common cause was drugs accounting for 13% cases. In this group, ART (VIROCOM-N) was responsible in 5/13 cases,

metformin in 2/13 cases, pantoprazole in 3/13 cases, phenytoin in 2/13 cases, and one case of sulfasalazine was found. Other etiological factors were tuberculosis (6/97), HIV (4/97), celiac disease (3/97), chronic pancreatitis (2/97), malaria (2/97), kalazar (2/97), ALL (1/97), hepatitis B (1/97), hypothyroidism (1/97), and tropical sprue (1/97).

Various Study Describing Causative Factors Similar To Our Study

Chanarin *et al.* reported diagnosis in 138 Indian patients with MA as, nutritional cobalamin deficiency in 69%, nutritional FA deficiency in 2% case, pernicious anemia in 15% cases, pregnancy in 2%, anticonvulsant therapy in 2%, blind loop syndrome in 2%, gastric carcinoma in 1% and 7% case were unevaluable. They also mentioned tuberculosis as associated disorder in 12% cases.^[14]

Unnikrishnan *et al.* reported nutritional deficiency in 26% cases and alcohol abuse in 13% cases as etiological factors for MA. They reported drug-induced MA in 13% and responsible drugs are phenytoin (4%), omeprazole (5%), and methotrexate (4%).^[8]

Khanduri *et al.* in their study reported 25% cases (30/120) of pantoprazole and ranitidine induced MA.^[7]

Britt *et al.* studied MA among Indians in Britain and found 68% cases of nutritional deficiency, 12% cases of pernicious anemia, and 20% cases of malabsorption. However, they did not mention the etiologic of malabsorption.^[13]

Matthews and Wood had studied the incidence of MA in Asians and found that 81% had nutritional deficiency and 19% had true pernicious anemia.^[13]

Lippi *et al.* performed a retrospective analysis to retrieve results of serum FA, B12, and TSH performed on outpatients and found 20% cases of FA deficiency and 6% cases of cobalamin deficiency in hypothyroidism.^[19]

Pradhan described the MA in case of malarial fever. They mentioned it is related to nitrous oxide and cobalamin interaction. However, exact prevalence is not mentioned. In our study, we found two cases of malarial fever with MA.^[20]

Nervo *et al.* suggested a prevalence of Vitamin B12 deficiency was 7% in metformin-treated diabetic patients in their study.^[21] Pflipsen *et al.* found a 22% prevalence of metabolically confirmed B₁₂ deficiency in the type 2 diabetic population taking metformin.^[22] However, we did not find any study on prevalence of metformin among MA as etiological factor.

Due to lack of facility available in the center, we did not consider “pernicious anemia” in our study; however, it is

the most common cause of MA described in many western literatures, but in India, the exact scenario of pernicious anemia is yet to be defined.

CONCLUSION

MA emerged as an important cause of morbidity and mortality in tropical countries, and increasing number of MA is seen in clinical practice over the past 10–15 years. It is very obvious that there is “resurgence” of articles on FA -B12 deficiency/MA over the past two decades.

In our study, there is a preponderance of young people. Hindu community is most commonly affected. Vegetarians especially vegans are most susceptible to MA especially cobalamin deficiency. Lacto-ovo vegetarian diet may protect from FA deficiency but not the from cobalamin deficiency. The pathological conditions associated with the MA are much diverse. Nutritional deficiency is the most common cause of MA, followed by alcohol and alcoholic liver disease. Other common causes are drugs induced and malabsorption (i.e. chronic pancreatitis, celiac disease, and tropical sprue) and chronic infections such as tuberculosis, HIV, and Kalazar. Hence, proper diagnostic workup is essential before the use of hematinic and blood transfusion in all patients of MA.

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Polycystic Ovary Syndrome Confers Additional Hormonal Level Abnormalities: A Study in Tertiary Care Hospital on Bengali Obese Women

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Abstract

Introduction: Polycystic ovary syndrome (PCOS) is one of the most frequently encountered endocrine disorders in women of reproductive age. Adiposity plays a crucial role in PCOS and influences the clinical and endocrine features in many women with this condition.

Purpose: This aim of the study was to compare hormonal abnormalities in women with obese Bengali PCOS cases attending in a government hospital with body mass index (BMI) matched women without PCOS in West Bengal.

Methods: A total of 75 obese PCOS patients (ethnic Bengali) were recruited and 75 BMI matched control were taken, and PCOS was diagnosis according to the Rotterdam criteria (2003). Serum follicle stimulating hormone (FSH), luteinizing hormone (LH), FSH/LH ratio, plasma glucose, insulin glucose/insulin ratio, and serum total testosterone were measured.

Results: Study serum LH, LH/FSH ratio, serum fasting insulin, and serum total testosterone levels were higher, and serum insulin/glucose ratio is lower than their obese BMI-matched controls.

Conclusion: Polycystic ovary syndrome confers additional hormonal level abnormalities in Bengali obese PCOS women in West Bengal.

Key words: Insulin resistance, Obese, Polycystic ovary syndrome

INTRODUCTION

Polycystic ovary syndrome refers to a multi-system reproductive-metabolical disorder, and it is characterized by irregular menstruation, hyperandrogenism, and polycystic ovarian morphology. It is most common endocrine disorder in women of reproductive age, and its prevalence of polycystic ovarian syndrome (PCOS) is 4–12%.^[1,2] Menstrual irregularity is characterized by irregular, infrequent, or absent menstrual bleeding.

PCOS is associated with obesity whether obesity causes PCOS or PCOS cause obesity is not clearly understood.

Obesity is a common finding in women with PCOS. Many women with PCOS (between 38% and 88%) are overweight^[3,4] the relationship between PCOS and obesity is complex, not well understood.

In obesity increased androgen production has been reported especially in women with upper-body obesity. Androgens play an important role in the determination of body composition. Chronic exposure to higher testosterone levels in women with PCOS may modify body fat distribution in these women. Support for this hypothesis is provided by studies of androgen administration in non-obese female to male transsexuals that lead to increases in visceral fat and adversely impact insulin sensitivity.^[5] There is considerable variation in body fat and fat-free mass among various ethnic groups. Many studies have suggested that Asian populations have more body fat relative to weight (but not in absolute terms) than white populations.

In Indians, receiver operating characteristic curve analysis showed a low sensitivity and negative predictive value of the

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conventional cutoff of body mass index (BMI) (25 kg/m^2) in identifications of overweight compared with a cutoff value based on percentage body fat, and this BMI cutoff resulted in substantial misclassification (approximately 25% of men and approximately 70% of women).^[6]

Obesity also causes the metabolic syndrome, which includes insulin resistance, type 2 diabetes mellitus. PCOS is also associated with insulin resistant.^[7,8] The presence of a defect in insulin action in PCOS has been described by many authors, but no clear study was done on Bengali women and few studies done in India to see the effect of obesity on PCOS with contrasting reports.^[9] Hence, the aim of the study is whether obesity has an additive effect on hormonal abnormalities such as insulin resistant or hyperandrogenism in PCOS cases or not.

Aims and Objectives

This aim of the study was to compare hormonal abnormalities in women with obese PCOS cases with BMI-matched women without PCOS in West Bengal so we can understand pathophysiology of PCOS better and improve management of PCOS.

METHODS

Study Design

A community-based case-control study was conducted from 2007 to 2011 among women aged 20–35 years who were permanent residents of West Bengal. PCOS patients with BMI ($\geq 30 < 35 \text{ kg/m}^2$) were recruited from the OPD clinics of the Department of Gynaecology in Institute of Postgraduate Medical Education and Research (IPGME and R), Kolkata. This clinical study was approved by the Institutional Ethics Committee (IPGME and R), Kolkata. All of the participants signed informed consent to be included in the study.

Sample Size

A total of 75 obese PCOS patients between age group between 20 and 35 years were recruited. Healthy age-matched controls ($n = 75$) women without PCOS and matched age, BMI recruited.

- Selection of cases and control from sources
- Operational definition
- Amenorrhea.

A patient who has been menstruating, the absence of periods for at least 3 of the previous cycle intervals or 6 months of amenorrhea.

Oligomenorrhea

Infrequent menstrual cycles at interval of more than 35 days. It is an indirect marker for anovulation in the absence of any hormonal evidence.

- Obese subjects
- Obese: BMI $30\text{--}35 \text{ kg/m}^2$
- Clinical hyperandrogenism
- Hirsutism, acne or alopecia.

Polycystic Ovaries

Polycystic ovaries was defined having follicles 2-9mm in diameter and ≥ 12 in number or ovarian volume $\geq 10 \text{ cm}^3$ in one or both ovaries on transabdominal pelvic ultrasonography (USG). There should be no dominant follicle with size greater than 10 mm in diameter.

Participant selected was undergone three stages of operation.

Stage I - questionnaire:

Administration of the questionnaire “Probable cases” and “probable controls” were identified during the cross-sectional survey.

A probable case: A “probable case” was defined as a woman with symptoms suggestive of PCOS (i.e., oligo/amenorrhea/ or clinical features of hyperandrogenism) as defined above.

A probable control: A “probable control” was defined as a woman with regular menses and no clinical features of hyperandrogenism. Probable control group matched for age and BMI with probable PCOS cases were selected. A detailed history of taking drugs was elucidated and all participants who were on oral contraceptive pills, oral hypoglycemic agents and antithyroid drugs were excluded from study. Desired number of control was selected.

They were then selected for Stage 2 examination.

Stage 2 - clinical examination and biochemical investigations.

Selected women were examined for the presence of hirsutism, acne, or alopecia. Hirsutism was routinely graded by two physicians independently using the common modified Ferriman -Gallway (FG) score. If the FG score differed by more than 2, re-evaluation by a third physician was done, and median values were used. Nine areas were examined - upper lip, chin, chest, upper abdomen, lower abdomen, upper back, lower back, thighs, and upper arms. Each area is scored 0–4, resulting in maximum score 36. Hirsutism was diagnosed when a score above 5 was evaluated.

Biochemical Investigations

Venous blood (5 mL) was drawn from both probable cases and probable controls. Blood samples were taken during the 3rd day of the menstrual cycle. Hemolyzed sera were discarded. Serum total testosterone was measured to diagnose biochemical

Table 1: Age and BMI of the study population

Age/BMI	Obese PCOS n=75	Obese controls n=75
Age in years		
Range	20–35	20–35
Mean	27.8	28.65
SD	3.4	2.7
BMI kg/m ²		
Range	30–35	30–35
Mean	31.08	30.98
SD	1.76	1.32

SD: Standard deviation, BMI: Body mass index, PCOS: Polycystic ovary syndrome

Table 2: Hormonal status of obese individuals with PCOS (BMI ≥30 <35 kg/m²) in comparison to BMI match controls and their statistical significance

Hormones	Mean±SD		P value, P, 0.05 significant
	Cases, n=75	Controls, n=75	
LH, mIU/mL	7.6±2.23	4.094±1.2	P<0.01, significant
FSH, mIU/mL	4.35±1.78	4.58±1.26	P=0.642, not significant
LH/FSH ratio	1.864±0.4	0.91±0.282	P<0.01, significant
Glucose, mg/dL	92±11.72	87±12.11	P=0.235, not significant
Insulin, uIU/mL	27.56±11.37	20.2±10.36	P<0.01, significant
Glucose/insulin ratio	4±2.36	5.58±2.48	P<0.01, significant
Total testosterone, ng/dL	99.07±34.15	18.27±11.42	P<0.01, significant

SD: Standard deviation, PCOS: Polycystic ovary syndrome, n: Number of cases, LH: Luteinizing hormone, FSH: Follicle stimulating hormone, BMI: Body mass index, PCOS: Polycystic ovary syndrome

Table 3: Correlation between BMI and another dependent variable in cases (P<0.05 is significant) n=75

Dependent variable	r value	P value
LH	-0.389	<0.01
FSH	-0.122	>0.1 NS
LH/FSH	-0.399	<0.01
Glucose	0.07	>0.05 NS
Insulin	0.545	<0.01
Glucose/insulin ratio	-0.38	<0.01
Testosterone	0.302	<0.01

NS: Not significant, LH: Luteinizing hormone, FSH: Follicle stimulating hormone, BMI: Body mass index

evidence of androgen excess or hyperandrogenemia. Hyperandrogenemia was diagnosed when serum total testosterone level was greater than 55 ng/dL. Upper normal level of serum total testosterone level was 55 ng/dL mentioned by kit supplier. Kit was supplied by Radio-pharmaceutical and isotope technology, BARC, Mumbai.

Stage 3 - ultrasound scanning.

Pelvic ultrasound scanning on women identified as probable cases and probable controls. Polycystic ovaries

on ultrasonography (USG) - multiple small follicles (>10–12) and (2–9 mm in diameter) tightly spaced along the periphery of the ovary.

Inclusion Criteria of Cases

The diagnostic criteria for PCOS were based on the unified standards formulated by the Rotterdam International Conference in 2003. Patients with any 2 of the following 3 conditions were diagnosed with PCOS: (1) Infrequent ovulation or anovulation; (2) hyperandrogenism or clinical manifestations of high blood androgen; (3) polycystic ovaries on USG - multiple small follicles (>10–12) and (2–9 mm in diameter) tightly spaced along the periphery of the ovary.

Exclusion criteria of cases included thyroid dysfunction, hyperprolactinemia, congenital adrenal hyperplasia, androgen-secreting tumors, Cushing syndrome, and other diseases.^[10]

Inclusion Criteria of Controls

Patients in the control groups exhibited normal menstruation, no clinical or biochemical signs of hyperandrogenism, normal ovaries as defined by ultrasonic examination and no family history of PCOS and they should be, age and BMI matched with cases.

Participants on OCP or conceived were excluded from the study. Chronic kidney disease, liver disease, cancer patients were also excluded from the study.

75 obese PCOS patients between age group between 20 and 35 years were recruited. Healthy age-matched controls (n = 75) women without PCOS and matched age, BMI recruited.

Other Biochemical Parameters

Blood samples were taken during the 3rd day of the menstrual cycle. Hemolyzed sera were discarded. All assays were completed within 3 days. Serum glucose estimation done by GOD-POD with kit manufactured by monozyme India limited, Secunderabad, insulin by radioimmunoassay with module supplied by Radio Pharmaceutical and Isotope Technology, Mumbai. Total serum follicle stimulating hormone (FSH) and luteinizing hormone (LH) were also measured.

Statistical Analysis

Statistical analysis was done by descriptive statistics in statistical analysis were carried out using Microsoft excel 2003. Descriptive statistics are presented as the mean ± standard deviation for normally-distributed variables. Student t-test was used to compare variables with normal distribution and P < 0.05 was considered significant.

RESULTS

Table 1 denotes basic characteristics of study groups. Difference between mean age and BMI of 75 obese PCOS cases and mean age obese controls are not statistically significant.

In Table 2 biochemical parameters were compared between PCOS and control group. In PCOS group serum LH level is (7.6 ± 2.33 vs. 4.094 ± 1.198 mIU/mL, $P < 0.0001$) higher than control. In PCOS group, serum FSH level is unaltered in relation to controls (4.35 ± 1.78 vs. 4.578 ± 1.26 mIU/mL, $P = 0.642$). In PCOS group, serum LH/FSH ratio level is higher than control (1.864 ± 0.4 vs. 0.913 ± 0.282 , $P < 0.001$). In PCOS group, serum fasting glucose level is unaltered in relation to control (87.4 ± 11.72 mg/dL vs. 92 ± 12.11 mg/dL, $P = 0.255$). In PCOS group, serum fasting insulin level is higher than control (27.56 ± 11.37 uIU/mL vs. 20.2 ± 10.36 uIU/mL, $P = 0.03$). PCOS group shows LOWER serum glucose/insulin ratio than control (4 ± 2.36 vs. 5.58 ± 2.48 , $P = 0.044$). In PCOS group serum total testosterone level is higher than control (99.07 ± 34.15 ng/dL vs. 18.27 ± 11.42 ng/dL, $P < 0.001$).

Table 3 denotes Correlation between BMI and other dependent variables in PCOS cases. BMI is negatively correlated with serum LH ($r = -0.389$, $P < 0.01$) serum LH/FSH ($r = -0.399$, $P < 0.01$) serum fasting insulin/glucose ($r = -0.38$, $P < 0.01$). BMI has no relation with serum FSH ($r = -0.122$, $P > 0.1$) and plasma glucose ($r = -0.07$, $P > 0.05$). Serum fasting insulin is positively correlated ($r = -0.545$, $P < 0.01$) with BMI.

DISCUSSION

In the present study, we evaluated the clinical and biochemical characteristics of women with polycystic ovary syndrome in West Bengal. To the best of our knowledge, this study is among few reports about clinical and biochemical features of PCOS in West Bengal. Multiple hormonal and metabolic abnormalities in PCOS are (1) gonadotrophin abnormality, (2) insulin resistance, and (3) sex steroid abnormalities.

Gonadotrophin Abnormality

In our study serum LH, LH/FSH ratio was higher than obese control. Elevated LH/FSH was found only 45% of obese cases. LH was negatively correlated ($r = 0.389$, $P < 0.01$) and LH/FSH was also negatively correlated ($r = 0.399$, $P < 0.01$). In our study, BMI is inversely correlated with serum LH concentration. In one study by Fulghesu *et al.* observed that altered basal concentration of serum LH was present on the

obese patient, but no relation with BMI is present. Negative correlation between BMI and LH which has been found by some authors suggest that leptin acting on a hypothalamic or pituitary level may dampen LH secretion in the obese state. Moreover, increased opioid tone and reduced dopaminergic tone have also described.

Insulin Resistance

Contrasting data exist about the importance of obesity in determining the insulin resistance in PCOS. Dunaif *et al.* demonstrated that insulin resistance in PCOS is associated with a unique cellular glucose transport defect independent of, but amplified by obesity. Earlier several articles also reported reduced insulin sensitivity in lean PCOS subjects^[11] whereas other authors reported that insulin resistance was entirely related to the adiposity in obese PCOS women and that hyperinsulinemia was secondary to other factors in lean patients (Mahabeer *et al.*, 1990p; Siegel *et al.*, 1990, Ciampelli *et al.*, 1997).^[12] It was demonstrated that the reduced response of glucose transport to a given concentration of insulin was greater in obese than in non-obese PCOS patients. Silfen 2003, observed that fasting insulin was significantly increased in the obese compared with the non-obese PCOS subjects. The obese adolescents with PCOS also demonstrated a greater insulin response to an oral glucose load compared with the non-obese PCOS group. All measures of insulin sensitivity, the I/G ratio was significantly reduced in the obese group compared with the non-obese PCOS group. The obese PCOS subjects compared with the obese controls, no statistically significant differences in glucose- and insulin-related parameters or the measures of insulin sensitivity were detected between the two obese groups. Hence, this study does not show an additive response. In another study, obese patients with PCOS have been shown to exhibit significantly more severe insulin resistance than obese women.^[13]

The bulk of these observations indicate that hyperinsulinemia in obese PCOS subjects is due to two factors: One characteristic of PCOS and the other obesity-specific. The mechanisms by which obesity may induce an insulin-resistance is enlargement of adipose tissue mass, in particular of the visceral fat depot, increases the availability of several metabolites, i.e. free fatty acids, lactate, etc., which are able to affect the secretion and the metabolism of insulin as well as its peripheral action.^[14] Insulin resistance in obesity can also be related to tumor necrosis factor (TNF- α) and leptin, both products of adipose tissue. TNF - mediates serine phosphorylation of IRS-1, which has been shown to interfere with the action of both insulin and IGF-I, by inhibiting insulin.

BMI does not accurately predict overweight in Asian Indians. Fat mass is high, so the endocrine response is exaggerated in obese PCOS cases. Further study is needed.

Sex Steroid Abnormality

PCOS patients with higher BMI seemed more likely to suffer hyperandrogenism or to exhibit the clinical signs of androgen excess.^[15] That is consistent with our study.

CONCLUSIONS

PCOS has been one of the most explored and controversial areas in reproductive medicine. It is a subject of continuous studies concerning both pathogenesis, diagnostics methods, and therapeutic procedures. It is associated with following endocrine abnormalities.

- Serum LH in obese PCOS is higher obese control while serum FSH level between two group. LH and LH/FSH ratio are positively correlated with BMI.
- Serum fasting insulin and total testosterone are higher in obese PCOS than obese control. From above data, we can conclude PCOS has an additive effect on endocrine abnormalities than obese control in Bengali women. PCOS *per se* has evolved as a risk factor for endocrinal derangements irrespective of the BMI status.

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Level of High-Sensitivity C-Reactive Protein Assay to Evaluate Risk in Follow-Up Patients with Acute Coronary Syndrome

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Abstract

Introduction: Among currently recognized inflammatory markers numbers of considerations favor high-sensitivity C-reactive protein (Hs-CRP) as a potentially useful predictor of prevalence and incidence of cardiovascular diseases. Clinical interest in these markers has also focused on their potential utility in predicting future cardiovascular events and thereby in patient's management.

Purpose of study: The purpose of the study was to determine the mean level of Hs-CRP assay in patients of acute coronary syndromes and correlation of Hs-CRP with two or more major risk factors and to correlate the level of Hs-CRP and cardiac events in patients of acute coronary syndromes during follow-up of a specified period of 6 months.

Materials and Methods: Present study had been carried out in the Department of Medicine, Gajra Raja Medical College and associated Hospital, Gwalior, Madhya Pradesh, India, from January 2004 to September 2005. This was a prospective observational study. The targeted populations were 30 cases with acute coronary syndromes of both sexes.

Results: The study was statistically insignificant in reference to various major cardiac events compared to various levels of Hs-CRP. ST elevation myocardial infarction (MI) was the most prevalent acute coronary syndrome. Most of the risk factors show their association with the moderate risk level of Hs-CRP, i.e., 1.0–3.0 mg/L, followed by high-risk levels, i.e., >3.0 mg/L, followed by low-risk levels, i.e., <1.0 mg/L. Post MI/angina was the major cardiac event that highest number of patients developed, during the follow-up period of 6 months.

Conclusion: No statistically significant association of various risk factors with Hs-CRP was observed in patients of acute coronary syndromes. No statistically significant association of Hs-CRP levels with major cardiac events was appreciable in patients of acute coronary syndrome in a follow-up period of 6 months.

Key words: Coronary syndrome, C-reactive protein, Myocardial infarction, Risk factor, Unstable angina

INTRODUCTION

In the current era, cardiovascular diseases (CVD) remain the leading cause of death worldwide.^[1] Although we do

not have exact national data on ischemic heart disease (IHD), it was found that the prevalence of CVD is increasing day by day, predominantly the incidence of coronary artery disease (CAD). The significance of the contribution of laboratory methods in clinical cardiology has grown in importance over the years. In recent time, the incorporation of biomarkers plays a major role for making new international guidelines and in the redefinition of myocardial infarction (MI). There are mainly two classes of indicators or markers of early cardiac cell injury and/or ischemia and marker of inflammation and coronary plaque instability and disruption.^[2]

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There are various serum cardiac biomarkers which associated with the acute coronary syndrome (ACS). The clinical application of cardiac biomarkers in ACS is no longer limited to establishing or refuting the diagnosis of myocardial necrosis. In association with electrocardiography (ECG) and clinical criteria, the cardiac biomarkers provide a convenient and non-invasive means to gain insights into the underlying causes and consequences of acute coronary syndrome that mediate the risk of recurrent events and may be targeted for specific treatment.^[2]

Biochemical cardiac markers play a major role for risk assessment in patients with an ongoing non-STsegment elevation ACS. Although the cardiac troponin-T, in particular, is generally recognized as an important risk indicator of underlying cardiac tissue damage, other markers of left ventricular performance (i.e., N-terminal pro-brain natriuretic peptide), inflammation (i.e., C-reactive protein), and renal function, i.e., estimated glomerular filtration rate are equally important in providing strong prognostic significance.^[3,4]

Since vascular inflammatory changes can hardly be evaluated using cardiac imaging methods, the role of inflammation biomarkers testing in peripheral blood is increasing, with the high sensitivity C-reactive protein (Hs-CRP) being the most profoundly studied in CVD. It remains stable in samples over long periods of time and can be quite simply, rapidly, and cheaply tested.^[1]

Multiple prospective cohort studies have shown the association between increased CRP levels and increased CVD event risk in patients with established disease, and the incidence of first cardiovascular events in individuals at risk for atherosclerosis.^[5]

It makes Hs-CRP testing valuable in both, primary and secondary CVD prophylaxis and for those, who already suffer from CVD. This test is useful in the evaluation of disease severity, treatment efficacy, and outcome prognosis.^[6,7]

MATERIALS AND METHODS

Place of Study

The present study had been carried out in the Department of Medicine, Gajra Raja Medical College and J.A group of Hospital, Gwalior, in the state of Madhya Pradesh, India, between the periods of January 2004–September 2005.

Aims and Objectives of the Study

The objectives are as follows:

1. To study the risk factors in patients of acute coronary syndromes.
2. To determine the mean level of Hs-CRP assay in patients of acute coronary syndromes.
3. To determine the correlation of Hs-CRP with two or more major risk factors.
4. To correlate the level of Hs-CRP and major cardiac events in patients of acute coronary syndromes, during follow-up of a specified period of 6 months.

Inclusion Criteria

The present study was included 30 cases of acute coronary syndromes, i.e., Unstable angina (UA), Non-ST-elevation myocardial infarction (NSTEMI), and ST-elevation myocardial infarction (STEMI). All the cases selected for the study were taken from the intensive care unit (ICU) of the Department of Medicine and J.A. Group of Hospitals at Gajra Raja Medical College, Gwalior, in the state of Madhya Pradesh, India.

Eligible patients had admitted with a typical history and chief complaint of anterior chest pain mainly at the retrosternal area which may radiate toward the left lateral side of chest and arm. Cases may have associated complaint of vomiting, breathlessness, palpitations, and sweating, etc. Cases were found positive for at least one cardiac marker of injuries such as CPK-MB or cardiac troponin-T (by Trop-T kit method) for NSTEMI and STEMI along with the typical ECG changes in support of CAD.

Exclusion Criteria

Following patients were excluded from the present study:

1. Patients taking estrogens/hormonal medications.
2. Patients with acute or chronic inflammatory conditions such as gingivitis, bronchitis, pneumonia, pancreatitis, and arthritis.
3. Patients already on aspirin, beta-blockers, niacin, and various statins therapy.
4. Patients on increased activity or endurance exercises.
5. Recent history of chest trauma.
6. Patients with valvular heart disease like rheumatic heart disease.
7. Cardiomyopathies and pericardial inflammatory diseases.

Laboratory Tests

All the relevant investigations have been done in the Department of Pathology, Radiology, and Cardiology, etc., of Gajra Raja Medical College and J.A group of Hospital, Gwalior, in the state of Madhya Pradesh, India.

1. Data from the clinical history, physical examination and ECG were recorded according to a fixed protocol.
2. The Hs-CRP estimation was done at the time of presentation, and the analysis was performed by turbidimetry immunoassay using QUANTA Reagent kit

(latex) manufactured by Tulip corporation, USA. Values of ≤ 1 mg/L, 1–3 mg/L, and >3 mg/L were labeled as low risk, intermediate risk, and high risk, respectively.

3. Complete blood picture,
4. Lipid profile.
5. Blood urea.
6. Serum creatinine.
7. Urine R/M.
8. X-Ray chest
9. 2-D Echo study.

All above-mentioned investigations were carried out by standard methods.

Patient's Diagnostic Criteria and Data Collection Method STEMI

1. Qualitative assay of cardiac troponin-T or CPK-MB positivity.
2. ECG showing pathological Q waves ($>$ or $= 0.04$ s in duration) and at least 20% reduction in amplitude of the following R wave.
3. ST-segment elevation of >1 mm in the limb leads or >2 mm in the precordial leads in at least 2 or more contiguous leads in a clinical setting of acute coronary syndromes.

UA and/or NSTEMI

TIMI-II Cass-A and B criteria for UA and Class-C for NSTEMI were followed which is as below:

1. Resting angina of at least 5 min duration, ST deviation ≥ 0.5 mm, and increased cardiac markers in case of NSTEMI.
2. New onset angina of at least Canadian cardiovascular classification Class III severity with onset within 2 months of presentation.
3. Previously diagnosed angina that became distinctly more frequent, longer in duration or lower in the threshold.

Major Cardiac Events were Recorded

1. Post-MI/ischemia angina.
2. Ventricular tachycardia (VT).
3. Re-myocardial infarction (Re-MI).
4. Atrioventricular blocks (AV-block).
5. Mortality.

All patients admitted in ICU with the fulfillment of above diagnostic criteria for acute coronary syndromes were

investigated thoroughly at the time of admission with all above-mentioned investigations including Hs-CRP. Patients were also inquired about other associated medical illnesses such as diabetes mellitus (DM), hypertension (HTn), cigarette smoking, and family history of cardiovascular events and obesity.

After discharge, all patients were kept in strict follow-up individually, for a specified period of 6 months from the date of discharge. Patients were asked to report from time to time and as and when needed strictly in person. Any major events from the above list were emphasized and if present, noted.

Statistical Analyses

The present study was a prospective observational study. Study data have been recorded using structured schedule (case report form) and entered for tabulation in Microsoft Excel Sheet. Statistical data were analyzed using statistical analysis system (SAS) for window version 9.1; SAS Institute North Carolina State University software. Statistical data were calculated by the frequency, percentage and mean \pm standard deviation and level of statistical significance were calculated with P -value (<0.05 significance) consideration.

RESULTS

Out of total $n = 30$ patients, $n^1 = 22$ cases were found male and remained $n^1 = 8$ cases female. The percentage of male patients was approximately $n = 22/30$, (73.33%) and that of females was $n = 8/30$, (26.67%). This data show the preponderance of male gender, which is consistent with the fact that it is male gender which is more susceptible to cardiovascular events. None of the patients was lost during follow-up period.

Age and Sex Distribution [Table 1]

The prevalence of acute coronary syndromes in various age groups in both males and females was as follows:

In Males

In the present study $n = 6/22$, 27.27% of male patients were belong to age group of 50–59 years which were followed by $n = 5/22$, 22.73% patients of age group between 40 and 49 years, this was subsequently followed by $n = 4/22$, 18.18% patients of age group 60–69 years,

Table 1: Age and sex distribution in cases of acute coronary syndromes

Sex ($n=30$)	Age in years ($n=30$)						
	0–29	30–39	40–49	50–59	60–69	70–79	80 and more
Male ($n^1=22$) (%)	0 (0)	3 (13.64)	5 (22.73)	6 (27.27)	4 (18.18)	3 (13.64)	1 (4.55)
Female ($n^1=8$) (%)	0 (0)	0 (12.5)	2 (25)	2 (25)	3 (37.5)	0 (0)	0 (0)

n : Total number of cases, n^1 : Number of cases according to sex

this, in turn, followed by $n = 3/22$, 13.64% patients of 70–79 years of age group, and $n = 3/22$, 13.64% patients belong to 30–39 years of age group. The second last prevalence was seen in $n = 1/22$, 4.55% patients in “80 and more” age group, ultimately followed by 0% patients in 0–29 years of age group.

In Females

The maximum percentage of the female patients $n = 3/8$, 37.50% belong to age group of 60–69 years which were followed by two groups simultaneously with equal prevalence $n = 2/8$, 25% in both 40–49 and 50–59 years age group, this was subsequently followed by $n = 1/8$, 12.5% patients from age group 30 to 39 years.

From Overall Patients

- Patients presented with UA - $n=8/30$, (26.67%).
- Patients presented with NSTEMI - $n=6/30$, (20%).
- Patients presented with STEMI - $n=16/30$, (53.33%).

The above results show that the maximum patients were presented with STEMI followed by UA which, in turn, followed by NSTEMI.

Symptomatology [Tables 2 and 3]

Chest pain described as most of the patients have retro-sternal and left-sided chest pain, few patients complaining radiation to the back also. Nitrates typically relieved the pain.

Males

Out of five presenting symptoms considered in the study, chest pain was the most prevalent symptom in males $n = 21/22$, (95.45%) which followed by palpitation $n = 15/22$, (68.18%) then by sweating $n = 15/22$, (68.18%), breathlessness $n = 11/22$, (50%) and ultimately vomiting $n = 6/22$, (27.27%).

Female

Out of five presenting symptoms the most prevalent symptom in females was chest pain $n = 7/8$, (87.50%), followed by palpitation $n = 6/8$, (75%) and sweating $n = 3/8$, (37.50%) which, in turn, followed by vomiting and breathlessness with $n = 2/8$, (25%) and $n = 1/8$, (12.50%), respectively.

- Total number of patients with chest pain - $n = 28/30$.
- Total number of patients with palpitation - $n = 21/30$.
- Total number of patients with sweating - $n = 18/30$.
- Total number of patients with breathlessness - $n = 12/30$.
- Total number of patients with vomiting - $n = 8/30$.

Overall, chest pain was the most common presenting symptom in all three classes of acute coronary syndrome $n = 8/30$, (87.5%) in UA, $n = 6/30$, (99.99%) in NSTEMI, and $n = 16/30$, (93.75%) in STEMI with mean value percentage (93.75%).

Hs-CRP level [Table 4]

- Total patients in low-risk group (<1 mg/L Hs-CRP level) - $n = 6/30$ (20%).
- Total patients in moderate risk group (1–3 mg/L Hs-CRP level) - $n = 14/30$ (46.67%).
- Total patients in high-risk group (>3 mg/L Hs-CRP level) - $n = 10/30$ (33.33%).

Male

In present study $n = 10/22$ (45.46%) of males showed moderate risk Hs-CRP levels followed by $n = 8/22$ (36.37%) patients were showing high-risk Hs-CRP levels and finally $n = 6/30$ (18.18%) of patients showing low-risk Hs-CRP levels.

Female

In present study $n = 4/8$, (50%) of females showed moderate risk Hs-CRP levels followed by patients showing high-risk and low-risk Hs-CRP levels $n = 2/8$, (25%) each.

Major risk factors [Table 5]

In the present study, following were the percentages wise distribution of the various major risk factors in overall acute coronary syndrome, as patients presented with more than one risk factor.

DM	16.67% (n=5)
HTn	23.33% (n=7)
Smoking	36.67% (n=11)
Hyperlipidemia	26.67% (n=8)
Family history	10% (n=3)
Obesity	13.33% (n=4)

Table 2: Incidence of various symptoms in patients with acute coronary syndromes

Sex (n=30)	Symptoms				
	Chest pain	Palpitation	Sweating	Breathlessness	Vomiting
Male (n ¹ =22)	21 (95.45)	15 (68.18)	15 (68.18)	11 (50)	6 (27.27)
Female (n ¹ =8)	7 (87.50)	6 (75)	3 (37.5)	1 (12.5)	2 (25)

n =total number of cases, n^1 =number of cases according to sex

In the present study, no statistically significant association of various major risk factors was observed with all three acute coronary syndromes mainly UA, NSTEMI, and STEMI, *P*-value of the risk factors was found statistically non-significant.

In the evaluation of the association of major risk factors with low, moderate, and high-risk levels of Hs-CRP following results were drawn out

DM

DM ($n = 5$) showed equal association with moderate and high-risk groups, i.e., $n=2/5$, 40% patients falling in each group, followed by $n = 1/5$, 20% patients in a low-risk group.

HTn

HTn ($n = 7$) showed maximum association with moderate risk group $n = 4/7$, (57.14%); followed by high-risk group $n = 3/7$, (42.80%) and finally the low-risk group $n = 2/7$, (28.57%).

Smoking

Smoking ($n = 11$) showed maximum association with moderate risk group with $n = 6/11$, 54.55% patients

followed by high-risk group with $n = 4/11$, (36.36%) and finally followed by low-risk group with $n = 1/11$, (9.09%).

Family History

The scenario with family history ($n = 3$) was different from other risk factors. In our study, it showed equal association with all three risk groups of Hs-CRP levels, i.e., $n = 1/3$, 33.34% patients in all three groups.

Obesity

The maximum association of obesity ($n = 4$) was observed with moderate risk group, i.e. $n = 2/4$, 50% patients followed by both low-risk group and high-risk group with $n = 1/4$, 25% patients each. “*P*” value (the value of significance) was more than 0.05 for all major risk factors, namely DM, HTn, smoking, family history, and obesity, which signifies that association of all Hs-CRP levels with all major risk factors was statistically insignificant, attributable largely to small study cohort, and short period of follow-up.

Major Cardiac Events [Table 6]

Post-MI/ischemia angina

Post-MI/ischemia was the most occurring major cardiac event in overall patients of the acute coronary syndrome (13.33%).

Incidence of post-MI/ischemia angina ($n = 4$) was the highest in high-risk group of Hs-CRP level with $n = 2/10$, 20% patients followed by $n = 1/6$, 16.67% patients in low-risk group and then ultimately moderate risk group with $n = 1/14$, 7.14% patients.

VT

There was virtually no incidence of VT in any risk groups of Hs-CRP levels.

Re-MI

In our study, 6.67% of overall patients of acute coronary syndrome developed Re-MI during the follow-up period of 6 months with equal incidence in both high-risk and low-risk groups.

Table 3: Frequency of various symptoms in different acute coronary events

Symptomatology ($n=30$)	UA ($n=8$)	STEMI ($n=16$)	NSTEMI ($n=6$)	MEAN %
Chest Pain	7 (87.5)	15 (93.75)	6 (99.99)	93.75
Palpitation	5 (62.5)	2 (68.75)	5 (83.35)	71.53
Sweating	5 (62.5)	2 (68.75)	2 (33.34)	54.86
Breathlessness	3 (37.50)	7 (43.75)	2 (33.34)	38.20
Vomiting	1 (12.5)	3 (18.75)	4 (66.67)	33.64

UA: Unstable angina, STEMI:ST-elevation myocardial infarction,
NSTEMI:Non-ST-elevation myocardial infarction

Table 4: Risk wise distribution of Hs-CRP assay in patients of acute coronary syndrome

Sex ($n=30$)	Hs-CRP		
	Low-risk <1 mg/L ($n=6$)	Moderate risk 1–3 mg/L ($n=14$)	High-risk >3 mg/L ($n=10$)
Male ($n^1=22$)	4 (18.18)	10 (45.46)	8 (36.37)
Female ($n^1=8$)	2 (25)	4 (50)	2 (25)

n =total number of cases, n^1 =number of cases according to sex.

Hs-CRP: High-sensitivity C-reactive protein

Table 5: Significance of post-infarct/ischemic events with special reference to the levels of Hs-CRP

Cardiac Events	Mild Risk ($n=6$)<1 mg/L	Moderate Risk ($n=14$)1–3 mg/L	High-Risk ($n=10$)>3 mg/L	<i>P</i>	Overall Incidence
Post-MI/ischemia angina	1 (16.67)	1 (7.14)	2 (20)	0.635	13.37
VT	0 (0)	0 (0)	0 (0)	-	0 (0)
Re-MI	0 (0)	1 (7.14)	1 (10)	0.73	6.67
Blocks	0 (0)	0 (0)	2 (20)	0.117	6.67
Mortality	0 (0)	1 (7.14)	1 (10)	0.736	6.67

Total number of patients having major cardiac events=10 (33.37%). Total number of patients having no major cardiac events=20 (66.67%). Hs-CRP: High-sensitivity C-reactive protein

Table 6: Distribution of major cardiac events in the follow-up period of 6 months in the patients of acute coronary syndromes

Sex (n=30)	Major Cardiac Events during 6 months follow-up period				
	Post-MI/ Ischemia Angina	VT	Re-MI	Blocks	Mortality
Male (n=22)	3 (13.64)	0 (0)	2 (9.09)	1 (4.55)	2 (9.09)
Female (n=8)	1 (12.5)	0 (0)	0 (0)	1 (12.5)	0 (0)

n=total number of cases, n'=number of cases according to sex. VT: Ventricular tachycardia, Re-MI: Re-myocardial infarction, Post-MI: Post-myocardial infarction

Mortality

Two cases among overall 30 patients suffered mortality; one case was from moderate risk group and another from high-risk group.

The overall incidence of mortality among all patients of the acute coronary syndrome was 6.67%.

Major cardiac events and corresponding Hs-CRP

Following results were drawn out:

Type of cardiac event	Mean Hs-CRP values (mg/L)
Post-MI/ischemic angina	2.50
Re-MI	2.865
AV-Blocks	3.68
Mortality	4.0

The mean value of Hs-CRP in major cardiac events group was 3.26 (mg/L) which is higher compared to the mean of no major cardiac events group 1.73 (mg/L); however, it is statistically insignificant ($P > 0.05$).

Taking the cutoff value 1 mg/L of hs-CRP we found that the

Sensitivity = 90% and Specificity = 25%

If taking the cutoff value of 3 mg/L of hs-CRP we found that the

Sensitivity = 40% and Specificity = 80%.

DISCUSSION

A total of total 30 patients, 22 cases were found male and remained 8 cases female. The percentage of males was approximately $n = 22/30$, (73.33%) and that of females $n = 8/30$, (26.67%). This data show the preponderance of male gender, which is consistent with the fact that it is male gender which is more susceptible to cardiovascular events. The maximum numbers of cases $n = 6/22$, 27.27% of males were belong to age group of 50–59 years.

Sharma *et al.* have been found in their study that from total 955 of patients those were admitted with a history of MI in 2 years of study periods, of which only 37 patients (3.9 %) fulfilled the inclusion criteria. The mean age was found 36.14 years, Male:female ratio was found to be 8:1, this data consistent with the present study.^[8]

Singh *et al.* have been observed in their study that, the highest number of cases was among 51–60 years (34.21%) and mean age of survived cases was 56.75 ± 10.47 . These findings were comparable to create registry and other two studies reported from Pakistan and Chennai study. The percentage of males was 76.58%, with male:female ratio 3.3:1 in this study. South Indian study noted that maximum anterior wall MI occurred among males (82%) with the male:female ratio 4.5:1. In North Bengal study, higher prevalence of CAD was noted among males. Male preponderance among STEMI cases in all age groups was observed in North India study.^[9]

Present study results show that the maximum patients were presented with STEMI followed by UA which, in turn, followed by NSTEMI.

T. Ohira, H studied that the acute coronary syndrome is now a leading cause of mortality in the Asia-Pacific region, accounting for around half of the global burden.^[10]

Xavier *et al.* have been found that the Indian patients with the acute coronary syndrome have a higher rate of STEMI (61%) than do patients in high-income countries (15-25%). India has the highest burden of ACS in the world and the create registry has provided contemporary data on 20,468 patients from 89 centers from 10 regions and 50 cities in India.^[11]

In the present study, maximum numbers of patients have associated risk factor as smoking followed by hyperlipidemia, HTn, DM, obesity, and family history. Our study results were consistent with the study of Sharma *et al.*^[8] as they have also been found the risk factors in their study patients as dyslipidemia, smoking, diabetes and HTn, and family history.

International Research Groups noted smoking or smokeless tobacco as a major risk factor for STEMI. In North Bengal study, the prevalence of IHD among smokers was significantly higher than in nonsmokers. Other published literature correlated smoking to be an important risk factor for CAD in Indian population.^[9]

Researchers from India reported less (7%) family history of among anterior wall myocardial infarction (AMI) cases. The rising incidence of ACS in Indians may be related to familial hereditary factors acting on modifiable risk factors, an important independent risk factor for CAD in younger cases.^[9]

Our study showed silent infarction in some patients with DM, although total percentage of DM was found to be 16.67%, the whole fact goes well. Rachel Hajar has also concluded that the DM patient has a high risk for cardiovascular disease development.^[12]

We have observed that the most common presenting symptoms in ACS cases were chest pain, palpitation, sweating, breathlessness, and vomiting, respectively. Chest pain among these found to be the most prevalent (93.75%), which was consistent with the study results of Cervellin and Rastelli.^[13]

In the present study, mean Hs-CRP level for major cardiac events group was 3.26 mg/L, which was much higher compared to 1.73% in the no major cardiac events group. Elevated Hs-CRP levels have been related to increased risk of death and MI. It was noted in present study that level of Hs-CRP was more with the aged patients, which were more susceptible to cardiovascular events, so there could be an indirect relation between Hs-CRP and cardiovascular events.

Patients having Hs-CRP value <1 mg/L were said to be at low risk, between 1 and 3 mg/L moderate risk and >3 mg/L are high-risk groups. Elevated levels of CRP in patients of acute coronary syndromes are approximately 5 times higher than stable individuals. In our study, being a noncomparative one did not measure the Hs-CRP level in normal patients; moreover, size of the cohort and small duration of follow-up was unlikely to give any significant results.

Karki *et al.* have been studied that the hs-CRP levels of >5 mg/L were found highly significant for predicting mortality during the hospital stay and at 6 weeks. In the GRACE registry, 12% of patients with STEMI, 13% with NSTEMI, and 8% with UA were expected to die in 6 months within the onset of symptoms. There have been a number of studies done which also found the prognostic significance of hs-CRP. Most of the studies were done in stable CAD. The JUPITER trial, which was restricted to participants with CRP levels >2 mg/L, found that treating the patients with rosuvastatin decreased the hs-CRP and low-density lipoprotein levels and finally the cardiovascular outcomes.^[14]

In our study, elevated levels of Hs-CRP were also noted with increasing age especially after 4th decade. Stone *et al.* have been also observed that the increased age has been shown to be associated with a significant increase in adverse outcomes in patients of UA/NSTEMI.^[15]

Ridker has observed that the acute phase reactant CRP as a simple downstream marker of inflammation has now emerged as a major cardiovascular risk factor.^[16]

Calabro *et al.* have been shown that CRP is composed of 523kD subunits and it is a circulating marker of pentraxin

family that plays a major role in the human immune system. Although it is primarily derived from liver, recent data indicate that cells within human coronary arteries particularly in the atherosclerotic intima can elaborate CRP.^[17]

Raised levels of CRP have been reported with poor prognosis in cases of UA in other study^[16] also, but in the present study no such association could be established along with this and there has been no statistically significant association of various risk factors, namely DM, HTn, smoking, obesity, hyperlipidemia, and family history with any of the acute coronary syndromes. Both these observations are largely attributable probably to the small-sized cohort and a very short period of follow-up.

The similar observations were noted by the Adukauskienė *et al.* in association of specified Hs-CRP levels with major cardiac events during the follow-up period; however, the mean Hs-CRP level of the patients suffering major cardiac events was higher than those who had no major cardiac events, but statistical significance is still lacking, probably again attributable largely to small cohort and short follow-up period.^[18]

So as a whole we know that Hs-CRP is a noble marker for prediction of risk because of its outstanding characteristics, this can be used as a routine tool for future risk estimation with excellent accuracy, as evidenced by Framingham Heart Study,^[19] but the present study does not support these findings, reasons are many but small-sized cohort and short follow-up period seem to be the most obvious culprits.

CONCLUSION

Here, finally, we concluded that:

1. The study was found statistically insignificant in reference to various major cardiac events compared to various levels of Hs-CRP.
2. The study was again found to be statistically insignificant in reference to different risk factors such as DM, HTn, smoking, hyperlipidemia, positive family history, and obesity compared to different acute coronary syndromes.
3. There was definitive male preponderance in the overall patients of various acute coronary syndromes.
4. The maximum numbers of patients were from 40 to 70 years age group both for the males and females.
5. Chest pain has been the most consistent symptom in overall patients, at the time of presentation to the ICU, both in males and females as well.
6. Smoking was the most consistent major risk factor associated with all acute coronary syndromes at the time of presentation.
7. Smoking was the major risk factor, which shows the maximum association with various levels of Hs-CRP.

8. In the present study, STEMI was the most prevalent acute coronary syndrome followed by UA and then by NSTEMI, among overall patients at the time of presentation.
9. Most of the risk factors had shown their association with the moderate risk level of Hs-CRP, i.e., 1.0 to 3.0 mg/L, followed by high-risk levels, i.e., >3.0 mg/L, and followed by low-risk levels, i.e., <1.0 mg/L.
10. Post-MI/ischemia angina was the major cardiac event that highest number of patients developed, during the follow-up period of 6 months. This was true for both males and females.
11. Total percentage of males developing major cardiac events, among overall patients were 26.67%, while total percentage of females developing major cardiac events among overall patients was 6.67%.
12. Among all major cardiac events, mortality was associated with highest concentrations of Hs-CRP.
13. The mean of Hs-CRP level of major cardiac events group was much higher than the mean of no major cardiac events group. The range of Hs-CRP levels from 0.14 to 5.1 mg/L; mean value = 2.23 mg/L.
14. No statistically significant association of various risk factors with Hs-CRP was observed in patients of acute coronary syndromes.
15. No statistically significant association of Hs-CRP levels with major cardiac events was appreciable in patients of the acute coronary syndrome in a follow-up period of 6 months.

Limitation of Study

The statistical insignificance in above study was probably attributable to small cohort under study and short duration of follow-up. This was a single center study with our limited resources.

Ethical Issues

The present study work has been conducted in the Department of Medicine and J.A. Group of Hospitals at Gajra Raja Medical College, Gwalior, in the state of Madhya Pradesh, India. The study work has been approved by the Institutional Ethics Committee.

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Amniotic Fluid Volume (q-AFV) Assessment for Intrauterine Growth Retardation in Hospital Settings

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Abstract

Background of the Study: Low amniotic fluid volume (AFV) observed to be a commonly associated finding with intrauterine growth retardation (IUGR), so the present study was planned to study the association of low AFV (single deepest pocket [SDP] <2 cm) and IUGR.

Materials and Methods: The study was conducted in tertiary care hospital of Himachal Pradesh, India, among 100 mothers with clinically suspected IUGR in 75 and normal growth in 25, which were followed up from 28 weeks of pregnancy till delivery.

Results: There is an insignificant odds ratio (OR: 3.7; 95.0% CI: 0.5–30.4) for insufficient AFV (SDP <2 cm) and clinical IUGR. There were four perinatal deaths in IUGR and none in normal group. Mean birth weight of baby was significantly more in normal group (3.0 kg) as compared to IUGR group (2.2 kg) ($P = 0.001$). Newborn was more active at the time of birth in normal group with average Apgar score of 7.2 in normal as compared to 5.9 in IUGR group ($P = 0.025$). In IUGR group, the Apgar score increased significantly up to 8.8 once the assessment was made at 10 min ($P = 0.000$).

Conclusion: AFV assessment will help as a facilitating tool for decision-making for the management of pregnancy rather substantiate itself as a sole tool with high predictive capacity.

Key words: Amniotic fluid volume, Intrauterine growth retardation, Pre-eclampsia

INTRODUCTION

Intrauterine growth retardation (IUGR) is associated with high perinatal mortality due to congenital malformation, intrapartum asphyxia, meconium aspiration, hyperviscosity, hypothermia, and hypoglycemia.^[1] Maternal health issues such as pregnancy-induced hypertension (PIH), diabetes mellitus, intrauterine infection, smoking, and poor nutrition are commonly observed to be associated with IUGR.^[2,3] Better coverage of ultrasonographic method does ensure qualitative assessment amniotic fluid volume (AFV) which has described as a method to screen IUGR in a case of

inadequate amniotic fluid. The presence of largest pocket of <1.0 cm perpendicular to uterine surface is considered as an indicative of insufficient AFV and of proxy to IUGR.^[2,4]

Amniotic fluid is mainly of fetal origin with some maternal contribution through placental membranes. At term, fetal swallowing results in the removal of fluid of about 500 mL in a day, whereas urinary excretion is about 500 mL/day by child. The bulk of exchange in amniotic sac is very rapid with a turn over equivalent to total fluid volume in every 2–3 h. The volume of fluid reaches to 100–150 mL by 15 weeks, and thereafter, there is a steady increase of approximately 1000 mL at 36–38 weeks of gestation.^[5,6] Clinical recognition of significant amniotic fluid changes is possible only in the second half of pregnancy and commonly occurs in last quarter of pregnancy. Oligohydramnios is a clinical hallmark of dysmature IUGR. It has been postulated that decreased production of fetal urine and insufficient breathing are associated with IUGR, so AFV assessment is determined

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by functional measure of IUGR. The present study was planned to study the presence of IUGR in accordance to AFV among mothers after 28 weeks' period of gestation (POG) till the time of delivery.

MATERIALS AND METHODS

The present study was conducted in tertiary care setting among 75 clinically suspected IUGR and 25 normal newborns in the third trimester of pregnancy (28 weeks onward). Clinical criteria for including a case with IUGR were The inclusion criteria for a case with IUGR were height of uterus 4 weeks less than the POG, stationary or falling maternal weight, serial measurement of abdominal girth showing stationary or falling values, and diminished amount of liquor amnii. Ultrasonographic examination was performed on RT 3000 (IGE India Ltd.) ultrasound using 3.5 MHz-phased array real-time transducer. Before examination, patient was asked to drink 24 ounces (720 mL) of fluid and refrain from voiding urine 3 h before the examination. The patient was examined in supine position with the application of non-greasy jelly, and examination was done with consistent serial sweeps in longitudinal and transverse planes. The largest amniotic fluid pocket was searched or measures in the vertical as well as transverse diameters. Classification of q-AFV was based on the smaller of the two diameters into the following three groups: Decreased (<1 cm), marginal (1–2 cm), and normal (2–8 cm). All mothers were followed up to 7 days of life for delivery with repeat q-AFV assessment, mode of delivery, birth weight of baby, Apgar score, and death.

RESULTS

A total of 100 pregnant women were included at 28 weeks of POG, of which 75 were clinically suspected for IUGR and rest 25 were normal, and these two groups have a mean age of 24.3 and 23.8 years, respectively ($P = 0.561$). Primiparity was insignificantly different in both IUGR and normal cases ($P = 0.222$). In both the groups, majority of pregnancy completed up to 39 weeks of POG, and an extension of pregnancy for 41 weeks was found only in IUGR group (1.3%). Maternal complications such as PIH were observed among 12 cases in IUGR and in 3 normal cases, and 3 cases were observed with heart disease in IUGR group. Complications during pregnancy and labor were assessed, and majority (IUGR: 77.3% and normal: 88.0%) of mothers and newborns had no complications in both the groups [Table 1]. There is an insignificant odds ratio (OR: 3.7; 95.0% CI: 0.5–30.4) for insufficient AFV (single deepest pocket [SDP] <2 cm) and clinical IUGR.

Table 1: Comparative assessment between clinically suspected pregnant mothers with IUGR and normal growth, Himachal Pradesh

Variable	IUGR (75)	Normal (25)	P value
Mean maternal age (+SD)	24.3 (3.9)	23.8 (3.1)	0.561
Primigravida (%)	37.3	24.0	0.222
Completed gestational age (%)			
38 week	53.8	44.0	0.418
39 week	28.0	28.0	1.000
40 week	17.3	28.0	0.248
41 week	1.3	0.0	NC
Mean birth weight in kg (+SD)	2.2 (0.2)	3.0 (0.3)	0.001
Mean APGAR score (+SD)			
5 min	5.9 (1.6)	7.2 (0.8)	0.025
10 min	8.8 (2.0)	9.7 (0.5)	0.061
Perinatal mortality/1000 LB	53.3	0.0	NC
AFV (%)			
Normal (2.0–8.0 cm)	86.7	96.0	0.356*
Marginal (1.0–2.0 cm)	10.7	4.0	NC
Decreased (<1.0 cm)	2.7	0.0	NC
Mean birth weight in kg (+SD) in q-AFV category			
Normal (2.0–8.0 cm)	2.2 (0.2)	3.0 (0.3)	0.001
Marginal (1.0–2.0 cm)	2.0 (0.5)	2.9 (NC)	NC
Decreased (<1.0 cm)	2.4 (NA)	-	NC

*Yates corrected Chi-square, NC: Not computed, IUGR: Intrauterine growth retardation, AFV: Amniotic fluid volume

Pre-eclampsia was observed in 16.0% and 12.0% of mothers in IUGR and normal group, respectively. Complications such as premature rupture of membranes (2), active inversion of the uterus (1), congenital malformation (1), pathological jaundice (2) and intrauterine demise (2) were observed in IUGR group only. A total of 55 pregnancies in IUGR and 16 in normal group delivered babies normally through vaginal route, whereas cesarean section was done in 16 mothers of IUGR and 9 mothers in normal group to deliver baby.

Mean birth weight of baby was significantly more in normal group (3.0 kg) as compared to IUGR group (2.2 kg) ($P = 0.001$). Newborn was more active at the time of birth in normal group with average Apgar score of 7.2 in normal as compared to 5.9 in IUGR group ($P = 0.025$). In IUGR group, the Apgar score increased significantly up to 8.8 once the assessment was made at 10 min ($P = 0.000$). There was a significant improvement in Apgar score from 7.2 to 9.7 at 5 and 10 min respectively in newborn of normal group [Table 1]. The mortality up to 7 days of life was observed only in IUGR group where a total of 4 deaths were observed: Two died in intrauterine, one due to birth asphyxia, and one due to septicemia.

Criteria laid that AFV showed that majority (IUGR: 86.7, and normal: 96.0%) of cases in both the groups were having normal amniotic fluid, whereas decreased amniotic fluid was observed only in IUGR (2.7%) group. Mean birth weight was significantly more in normal (3.0 and 2.9 kg)

as compare to IUGR group (2.2 and 2.0 kg) in cases with normal and marginal AFV. No case was observed with decrease AFV in normal group, whereas it was observed in IUGR group with mean birth weight of 2.4 kg which is relatively more than the marginal AFV due to less number of cases (only 2) [Table 1].

Majority of mothers had normal AFV when assessed and the frequency distribution across POG from 28 to 40 weeks showed an increase for normal AFV in IUGR group after 35 weeks, whereas the fraction increased from 32 weeks of POG for normal AFV in normal group [Figure 1]. Prolonging labor in IUGR group, therefore, holds potential for an increase in AFV in the latter half of the pregnancy.

DISCUSSION

AFV considered as a functional indicator for IUGR and its repeat assessment over a period of time gives an idea about intrauterine baby growth. The present study was planned to assess any association between insufficient AFVs with growth retardation. The present study observed 3 times odds (OR: 3.7; 95.0% CI: 0.5–30.4), but statistically insignificant, of insufficient AFV (SDP <2 cm) among clinically IUGR babies. In IUGR group, the present study showed a presence of suboptimal (<2 cm) AFV in 13.4%, whereas very low AFV (<1 cm) in 2.7% mothers. Birth weight as an outcome was assessed for less intrauterine growth and found that, in IUGR group, it was significantly (2.2 vs. 3.0 kg) lower than the normal group. All mothers delivered at tertiary care hospital and timely newborn care observed a significant improvement in Apgar from 5 to 10 min of life along with four deaths in perinatal period in IUGR group. Of these four, all 4 deaths were observed among women with normal and marginal AFV and none in women with decreased AFV (SDP <1 cm). Relatively low

birth weight in women with normal AFV in IUGR group along with deaths did not support AFV as a functional indicator for screening growth retardation and perinatal death. Repeat assessment observed that, over a period of time (from 28 to 40 weeks) in both IUGR and normal groups, majority of mother become normal for AFV (2–8 cm) and only 2 mothers had very low AFV (<1 cm) and 8 has marginal (1–2 cm).

Evidence has demonstrated the predictive efficacy of AFV for IUGR as poor measure where amniotic fluid was measured by diazo-dye reaction.^[7] In a study among 1038 women where amniotic fluid index (AFI) of more than 5.0 cm as quoted earlier, it turned out to be a poor screening test for small for gestational age fetus.^[8] Effect of oligohydramnios in uncomplicated pregnancies was assessed and observed a significant association between AFI, 5 cm, and low birth weight (OR: 2.2, 95% CI: 1.5–3.2).^[9] An assessment among 1393 pregnant women over 12 months' period observed no statistical significant association between AFI and estimated fetal weight with a conclusion that the fluid volume and index shows variations in the late half of the pregnancy which is non linear with the amniotic volume, index and fetal weight.^[10]

Argument has placed that measuring amniotic fluid pockets is a reasonably reliable method to predict perinatal mortality with commonly used criteria of SDP <2 cm and AFI <5 cm, where before 34 weeks, AFI of <5 cm is a criteria for intensive fetal monitoring though it has greater sensitivity and precision but poor predictor of perinatal mortality. After 34 weeks, the use of either AFI or AFV assessment can expect to identify high-risk fetus reliably if repeat measurements are confirmatory.^[11] Concordance to the present study evidence did observe AFV, specifically oligohydramnios as a poor predictor for perinatal mortality.^[12] With a changing nutrition profile of

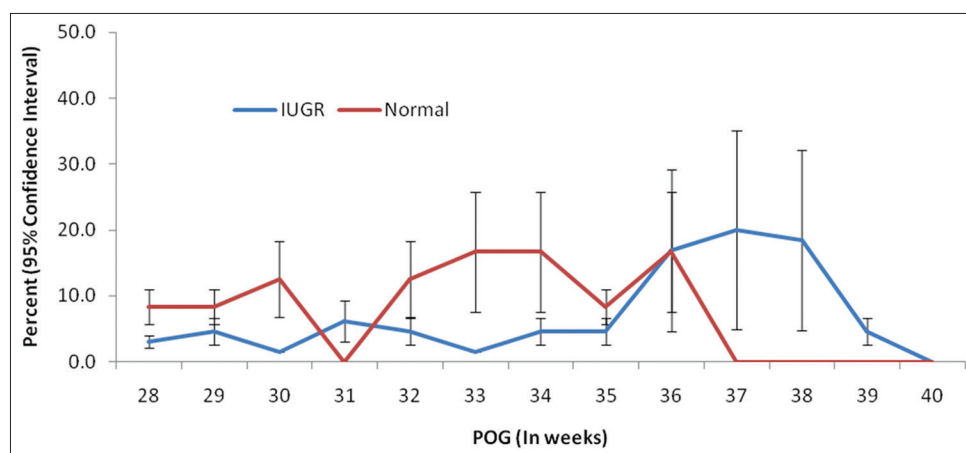


Figure 1: Comparative trend for normal amniotic fluid volume over period of gestation between clinically suspected pregnant mothers with intrauterine growth retardation and normal growth, Himachal Pradesh

and compliance, the bed rest recommended to mother over the period of pregnancy expects an improvement in AFV; therefore, follow-up assessment of AFV is recommended. Repeat assessment for AFV to decide the utility of volume as a prognostic indicator was also assessed in low-risk pregnancies, and finally, it was concluded that the repeat assessment has no prognostic significance.^[13]

Method of assessment and subjective variations does influence the interpretation of findings and decision-making process. A study to assess the AFI and SDP as best technique was conducted where six publications compared the two and 21 had contained both techniques, it was found that AFI identified significantly greater number of women with oligohydramnios but without any difference with perinatal outcomes. AFI observed to over classify women with oligohydramnios with unwarranted interventions; therefore, AFI was recommended to be abandoned as a measure, rather preferred to use SDP to assess AFV.^[14] Amniotic fluid may have a poor prediction due to changing volume over a pregnancy period which depends on fetus renal function and respiration along with mother nutritional status, but its implications in resource-poor settings warrant close monitoring as an adjunct for intrauterine growth monitoring of child and look for the presence of congenital anomalies.^[15] AFV assessment will help as a facilitating tool for decision-making for the management of pregnancy rather substantiate itself as a sole tool with high predictive capacity. The current study has methodological limitations in a way where unequal distribution of pregnancies 75 and 25 in IUGR and normal group, respectively, without sample size estimation. The sample size distributed differentially and skewed which is evident from wide CI of odds ratio, a matched case-control study would have been better with 1:1 ratio. In addition, the present study had not considered AFI as an adjunct measure.

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Evaluation of Subject Response to Antipsychotics - Subjective Aspect and Related Clinical Correlates

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Abstract

Aim: The aim of this study is to assess the subjective response to antipsychotics in patients with schizophrenia and to assess the related factors such as psychopathology, side effects, insight, and treatment variables.

Methodology: A total of 60 patients with schizophrenia were randomized to treatment with risperidone (n=30) or haloperidol (n = 30) daily. Efficacy was assessed by the improvement of psychotic symptoms, measured on the positive and negative syndrome scale. The safety and tolerability were evaluated with the extrapyramidal symptom rating scale, the UKU side effect rating scale, and Insight and Treatment Attitude Questionnaire.

Results: Comparing haloperidol group and risperidone group for variables such as sex, age, duration of treatment, literacy level, and drug-free duration before admission was not statistically significant. Hence, both groups are comparable. Haloperidol group had the number of dysphoric patients (21), and risperidone group had only 8 patients who had dysphoria (Chi-square $P < 0.01$). In psychopathology, subjective response was more dysphoric when paranoid scores were high (significant two-tailed -0.00). In the final assessment total, psychopathology scores were high if dysphoria is high and if psychopathology scores were low and the dysphoria is also low (significant two-tailed -0.00). Dysphoria scores are high if insight is low, and dysphoria scores are low if insight is good. Dysphoria scores increase with increasing side effects and decrease with decreasing insight (significant two-tailed -0.00).

Conclusion: Subjective response to risperidone is better than haloperidol. If there is the initial dysphoric response, the treatment response is reduced with low insight and high psychopathology in the dysphoric group.

Key words: Antipsychotic therapy, Insight, Schizophrenia

INTRODUCTION

Schizophrenia has consistently attracted the attention of psychiatrists and neurologists throughout the history of the disorder because of the magnitude of its clinical problem. With improved drug treatments, the area that evinces interest in schizophrenia factors affects the outcome of treatment and relapse. With the introduction

of chlorpromazine and haloperidol, there came a revolution in the treatment of patients with schizophrenia. With the introduction of more and more newer antipsychotics, the trend is more toward subjective tolerability and quality of life with antipsychotics.

The relevance of subjective response to medications was raised by Sarwer-Foner in the early 1960s itself (George Awad – 1993). The psychological and psychodynamic issues in influencing drug response are gaining interest recently. The effect of subjective response originated when patients receiving antipsychotics complained that medications are worsening their condition even clinically their symptoms reduced. Later, it was found that patients receiving neuroleptics with the complaints of dysphoria when followed up showed that they had a less favorable outcome

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to treatment than the group of patients without dysphoria.^[1-5]

Further studies proved that the side effects did not influence the subjective response. The severity of psychopathology had the varied influence on the subjective response. Paranoid states, depression, and negative symptoms also influenced the subjective response to antipsychotics.^[6] SPET and PET studies have proved that patients who experience dysphoria had increased binding of dopamine receptors (D2) in the nigrostriatal region.^[7] It implies that patient with lower dopamine activities is likely to develop dysphoria. For these reasons, the newer antipsychotics are tolerated better, and patients express favorable subjective response.

The implications to the clinicians are that patients who develop dysphoria to a drug consider changing the drug or the drug dosage should be reduced. Days have changed from isolation and chaining of mentally ill to optimizing the objective and subjective improvement, thereby the quality of life. We ask patients with schizophrenia many questions, but we never ask them whether the medication produces any unpleasant response in them. With the identification of the subjective state, the pharmacotherapy in schizophrenia sees that a new world is exploding in the factors influencing compliance to therapy.

Aim

The aim of this study is to assess the subjective response to antipsychotics in patients with schizophrenia and to assess related factors such as psychopathology, side effects, insight, and treatment variables.

METHODOLOGY

This prospective observational study was conducted in the Department of Psychiatric. A total of 60 consecutive patients with a diagnosis of schizophrenia were screened from the patients getting admitted as inpatients. They were selected based on inclusion and exclusion criteria. Written consent was obtained from the patients and relatives for this study. All subjects gave written consent to participate in the study. Cases were diagnosed as schizophrenia by the investigator based on ICD-10 criteria. All consecutive patients who satisfied the inclusion and exclusion criteria were enrolled into the study. The investigator was blind to the antipsychotic drug used. The treating clinician gave the prescription. Of these 60 patients who gave consent, 6 patients withdrew within a week due to personal reasons and requested to be discharged. Patients were given either haloperidol or risperidone. Odd-numbered patients received haloperidol and even-numbered patients received risperidone. The first assessment was done on the 1st day, and final evaluation was done on the 14th day.

In few patients, it was done few days before itself as they requested to be discharged. Patients were maintained on one antipsychotic, and other oral medications were not given. Anticholinergics were started whenever indicated. Injection lorazepam was used in agitated patients. The antipsychotic dosage was not fixed, and it was titrated based on the daily clinical evaluation. ECT was not given.

Inclusion Criteria

The following criteria were included in the study:

1. Patients with a diagnosis of schizophrenia based on ICD-10 criteria.
2. Patients who were drug free for 4 weeks or drug naïve.
3. Age between 15 and 45 years.
4. Giving consent for the study.

Exclusion Criteria

The following criteria were excluded from the study:

1. Comorbid substance abuse amounting to dependence
2. Significant medical and neurological illness
3. Comorbid psychiatric disorders.

The tests were administered by a single rater, and approximate duration for administering all the tests for an individual is 1–1 ½ h and was conducted in a single session. The second assessment was done on 14th day after starting treatment.

Instruments Used

1. Semi-structured pro forma for sociodemographic details and illness details.
2. PANSS - positive and negative syndrome scale
3. DAI - drug attitude inventory
4. The UKU side effect rating scale
5. ITAQ - insight and treatment attitude questionnaire.

RESULTS AND DISCUSSION

Of the 60 patients who gave consent, 6 patients withdrew within few days and requested to be discharged for personal reasons. Hence, the final sample size was 54, i.e., 27 in haloperidol group and 27 in risperidone group.

Chi-square test was used to find the significant difference between haloperidol and risperidone and found not statistically significant for variables - sex, age, duration of illness, previous treatment, literacy level, drug free duration before the study. Hence, the cases in both the groups are comparable.

Of the patients receiving haloperidol, one patient opted to get discharged early due to these reasons. Five patients (18.5%) in haloperidol group and three patients in risperidone (11.11%) group wanted to get discharged

on the 12th day. They could not be asked to come for the assessment on the 14th day, as they are from distant places. The second assessment was done on the 12th day itself. In the haloperidol group, 77.7% and, in risperidone group, 85.2% completed the stipulated 14 days. However, the difference was not statistically significant [Table 1].

Whenever patients developed extrapyramidal side effects, of which dystonia was more frequent, patients were started on the anticholinergic drug. The number of patients in haloperidol group 40.7% had to receive anticholinergic when compared to 3.7% in risperidone group. The difference was statistically significant when Chi-square test was applied ($P < 0.01$).

PANSS, UKU, and DAI difference was found out for each (before Rx minus 14 days of Rx). Mean was calculated for these differences for 2 drugs separately. The *t*-test was used to find the difference between these mean.

For all measures, i.e., DAI, PANSS from 1 to 9, ITAQ, and UKU, the difference between the 1st-day observation and last observation was calculated separately for each patient. The difference was added up, and the mean was calculated. The haloperidol group and the risperidone group were compared using the *t*-test for equality of means.

Results were that there was no statistically significant difference in two groups regarding changes after pharmacotherapy in subjective response, psychopathology, and insight scores. Hence, the effect of two drugs was comparable in 2 weeks' period. Regarding side effects, haloperidol group had significant change, i.e., increase in side effects which were statistically significant when compared to risperidone group.

All the variables DAI, PANSS 1-9, ITAQ, and UKU for the first assessment were compared between the two groups, i.e., haloperidol- and risperidone-receiving groups.

There was statistically significant difference in the subjective response (DAI) score, i.e. haloperidol group ($P = 0.00$) (mean - 2.89) significantly dysphoric when compared to risperidone group (mean + 0.7).

In the PANSS score - negative syndrome and anergia scores, there was a statistically significant difference, i.e. scores are significantly more in risperidone group. Other measure in PANSS, there was no significant difference. Hence, the patients were distributed in both the groups in a comparable way.

In the insight (ITAQ) and side effects (UKU scores), there was no statistically significant difference in both haloperidol and risperidone groups for the day-1 assessment.

All the variables DAI, PANSS 1-9, ITAQ, and UKU for the second assessment were compared between haloperidol and risperidone group.

In the second assessment also, the subjective response (DAI) was dysphoric in the haloperidol group when compared to risperidone group, and the difference was statistically significant.

In the UKU scale, scores (side effects) were statistically significant in the haloperidol group when compared to risperidone group. The difference was more significant in psychic and neurologic side effects [Table 2].

To find whether anticholinergic drugs used had produced the significant change in subjective response, the Chi-square test was applied. There was no statistically significant difference between the groups (i.e., received and not received).

The subjective response was negatively correlated with psychopathology (PAN2-124 positive, negative, and general psychopathology added together), i.e., when psychopathology was high, the subjective response was negative (dysphoric), and when psychopathology was low, the subjective response was positive (non-dysphoric).

The subjective response was inversely correlated with side effects, paranoid score, i.e., when the subjective response was dysphoric (low score) side effects and the paranoid score was high. When the subjective response was non-dysphoric (high score) the, side effects and paranoid scores were low.

This shows that haloperidol group had the number of dysphoric patients (dysphoric-21, non-dysphoric-6) and risperidone group had the lower number of dysphoric patients (dysphoric-8, non-dysphoric 19).

When Chi-square test was applied, there was a significant difference ($P < 0.01$) indicating haloperidol produced significant dysphoric responses.

Table 1: Comparison between the haloperidol group and risperidone group on the scores of first assessment

Scales	t-test for equality of means			
	t	df	Significant (two-tailed)	Mean difference
DAI1	-3.46	52	0.00**	-3.63
UKU1P	-0.14	52	0.89	-0.07
UKU1N	0.45	52	0.66	0.04
UKU1A	-1.95	52	0.06	-0.37
UKU1O	-1.44	52	0.16	-0.07

** $P < 0.01$, * $P < 0.05$

Table 2: Comparison of dysphoric and non-dysphoric group

Characteristics	Independent samples t-test for the equality of means			
	t	df	Significant (two-tailed)	Mean difference
Age	2.99	52	0.00	5.00
Mean duration of illness	2.18	52	0.03	2.91
Mean psychopathology on the first assessment	-0.27	52	0.79	-0.88
Side effects - final assessment	2.80	52	0.01	2.29
Mean insight - first assessment	-3.05	52	0.00	-4.36
Mean difference in psychopathology	1.54	52	0.13	4.63

In the sex distribution, there was no significant difference between male and female patients. (Chi-square test - $P = 0.777$).

The subjective response rating was on the first assessment. The mean age in the dysphoric group was 33, and the non-dysphoric group was 28 which had the significant difference ($P < 0.00$).

Mean duration of illness in the dysphoric group was 7.43 years and the non-dysphoric group was 4.52 years which had less significance.

The initial mean psychopathology scores were not significantly different in both the groups. The mean difference in psychopathology scores also did not significantly differ in both the groups [Table 3].

The initial dysphoric subjective response was significantly ($P = 0.01$) associated with the increase in side effects. There was a significant difference in mean insight between the dysphoric and non-dysphoric groups. The dysphoric group had lower mean insight (4.48) than the non-dysphoric group (8.84).

The subjective response was dysphoric (negative) when haloperidol was given. The findings of Van Putten and May 1978 and Awad and Hogan 1985 were replicated. Risperidone had the positive subjective response.^[3,4] The findings of Voruganti *et al.* 2002 and Hellewell *et al.* 1999 were replicated.^[8,9] The haloperidol and risperidone group was comparable in age, sex, literacy, duration of illness, and previous treatment. Haloperidol-receiving patients were more often receiving anticholinergics than risperidone-receiving patients. The side effects at the end of 2 weeks observation were also high in the haloperidol group than risperidone group. This shows that risperidone has advantages over haloperidol in subjective response, side effects, and the need for anticholinergics [Table 4].

Dysphoric respondents had significantly low insight at the onset of treatment. They had more side effects on follow-up [Table 5]. The findings of Rossi *et al.* 2000 are replicated.^[10] The findings of Gervin *et al.* 1999 have been replicated as subjective response inversely correlated with

side effects. The non-dysphoric group had significantly better insight and less.^[11]

The psychopathology did not significantly vary between the two groups. 2 weeks' observation was brief. To establish a difference, a longer duration of observation is needed. Hence, the findings of Van Putten and May 1978 and Hogan and Awad 1980 could not be replicated.^[3,12] Other aspects of psychopathology were related to subjective response in that higher the psychopathology more the dysphoric response. If paranoid ideation was high, the subjective response becomes more dysphoric. The subjective response correlated with the total psychopathology paranoid score. The findings of Cabeza *et al.* 2000 were replicated. The subjective response was not altered by the addition of anticholinergic.^[13] The findings of Rossi *et al.* 2000 is replicated.^[10]

CONCLUSION

The subjective response is correlated with treatment variable. Haloperidol has more dysphoric response, and risperidone has the non-dysphoric response. This confirms the advantage of risperidone over haloperidol. The subjective response is negatively correlated with psychopathology, side effects. As the psychopathology increases, the dysphoria increases. The subjective response is correlated with insight. Dysphoric responders have more side effects at the end of observation. Hence, if there is any dysphoric response to a particular antipsychotic soon after starting the drug it indicates that he may become a poor

Table 3: Comparison between the haloperidol group and risperidone group for the score on the second assessment

Scales	t-test for equality of means			
	t	df	Significant two-tailed)	Mean difference
DAI2	-2.54	52	0.01**	-2.59
UKU2P	2.77	52	0.01**	1.19
UKU2N	4.19	52	0.00**	1.15
UKU2A	0.65	52	0.52	0.22
UKU2O	1.21	52	0.23	0.11

** $P < 0.01$, * $P < 0.05$

Table 4: Correlation between subjective response and other variables at the final observation

Subjective response	Psychopathology	Insight	Negative syndrome	Depression	Side effect	Paranoid
Pearson correlation	-0.407	0.153	0.034	-0.011	-0.413	-0.43
Significant (two-tailed)	0.002	0.270	0.807	0.935	0.002	0.00

Table 5: Frequency distribution of antipsychotics in dysphoric and non-dysphoric group

Drug	Count (%)		
	Dysphoric	Non-dysphoric	Total
Haloperidol	21 (71.41)	6 (24)	27 (50)
Risperidone	8 (27.59)	19 (76)	27 (50)
Total	29 (100.00)	25 (100)	54 (100.00)

P<0.01

responder to that drug with more side effects. Hence, the clinician can consider another drug which will improve the subjective response and thereby compliance. In addition to all other factors influencing compliance in patients with schizophrenia, the role of subjective response also should be given importance by the clinician.

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Imaging Characteristics of Focal Liver Lesions on Contrast-Enhanced Helical Computed Tomography

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Abstract

Introduction: The discovery of computed tomography (CT) by G.N. Hounsfield in 1972 has been a milestone in medical diagnostic imaging as cross-sectional imaging took a step into diagnostic radiology. The use of contrast agents for CT of the liver has been used since long back. However, the advent of multidetector helical CT has made the dream of multiphasic imaging a reality. This has led to imaging the liver during the various phases of enhancement and helping in characterization and detection of the lesions.

Material and methods: This prospective study was done in the Department of Radiodiagnosis and Imaging at Bhopal Medical Centre, Bhopal, Madhya Pradesh, India. A total of 100 patients who were referred to our department with strong clinical suspicion of focal liver lesion and those diagnosed by ultrasonography underwent multiphasic contrast-enhanced CT evaluation of abdomen using single-slice spiral CT scanner from March 2010 to May 2012.

Results: In our study, the majority of cases diagnosed were that of malignant lesions in 47% of cases. The other lesions diagnosed were benign lesions in 34% of cases and inflammatory lesions in 19% of cases. Among the malignant lesions, the most common diagnosis was that of metastases seen in 67% of cases. The next most common was hepatocellular carcinoma (HCC) seen in 29% of cases.

Discussion: Contrast-enhanced multiphasic CT plays an indispensable role in the detection and characterization of focal lesions of the liver. The aspects of the identified liver abnormalities influence the clinical and surgical decision-making. Benign abnormalities such as cysts and hemangioma do not require treatment, but some benign cases require treatment such as FNH and hepatocellular adenoma requires treatment in some cases. Malignant lesions arising from the liver such as HCC often need treatment. Metastases may or may not be amenable to treatment.

Conclusion: The accuracy of contrast-enhanced multiphasic CT in detecting and characterizing focal liver lesions is high, and it should be considered in the imaging workup of any patient with focal liver lesions. This helps in guiding further management of these patients avoiding unnecessary investigations and workup for the diagnosis as there is a high incidence of benign pathologies in the liver.

Key words: Benign, Contrast-enhanced helical computed tomography, Hepatic, Malignant

INTRODUCTION

Liver is the largest organ of the human body and being a filter in the body is plagued by a variety of focal and diffuse pathologies. As it is one of the most common locales for

the spread of malignant diseases, the liver is the abdominal organ of greatest interest for imaging studies.

The discovery of computed tomography (CT) by G.N. Hounsfield in 1972 has been a milestone in medical diagnostic imaging as cross-sectional imaging took a step into diagnostic radiology. The use of contrast agents for CT of the liver has been used since long back. However, the advent of multidetector helical CT has made the dream of multiphasic imaging a reality. This has led to imaging the liver during the various phases of enhancement and helping in characterization and detection of the lesions.

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The increased speed of scanning, the absence of respiratory misregistration artifacts due to single breathhold scanning ability to reconstruct thin slices retrospectively, and multiplanar reconstruction capability in sagittal and coronal have made multiphasic scanning taking a giant leap in the characterization of focal liver lesions by non-invasive means.

Although the recent evolution of diagnostic radiologic technologies has changed the setting of hepatic imaging, misdiagnoses during early disease development may prevent patients from obtaining advantageous management. There is an insufficient diagnostic performance for both the early detection and the characterization of small liver lesions even with CT and magnetic resonance (MR) imaging techniques. As such, there is a need to improve on morphology-based CT and MR imaging using contrast agents for the early detection and characterization of hepatic disease.^[1-3]

MATERIALS AND METHODS

This prospective study was done in the Department of Radiodiagnosis and Imaging at Bhopal Medical Centre, Bhopal, Madhya Pradesh, India. A total of 100 patients who were referred to our department with strong clinical suspicion of focal liver lesion and those diagnosed by ultrasonography underwent multiphasic contrast-enhanced CT evaluation of the abdomen using single-slice spiral CT scanner from March 2010 to May 2012.

Inclusion Criteria

The following criteria were included in the study:

- Patients referred to the Radiodiagnosis Department of Bhopal Medical Centre, Bhopal, with strong clinical suspicion of focal lesion of liver including those with primary malignancy elsewhere.
- Patients already diagnosed with focal liver lesion by ultrasonography.

Exclusion Criteria

The following criteria were excluded from the study:

- Patients with diffuse liver diseases.
- Patients with mass lesions infiltrating the liver from outside the liver.
- Patients with traumatic injury to liver.

Procedure

After obtaining the written consent from all the participants under the study, detailed history of the patient including signs and symptoms, detailed physical examination, biochemical investigations, and radiological investigations which included chest X-ray and ultrasonography of the abdomen were recorded.

The liver was viewed in non-contrast-enhanced phase, arterial phase, portal venous phase, and delayed phase in axial, sagittal, and coronal sections and any abnormality was identified. When multiple lesions are noted, the most representative lesion or the largest of the lesions was taken into consideration. When different types of lesions were identified in the same person, representative lesions of each type were considered. The following characteristics of the lesions were noted.

- The number of lesions.
- The segmental location of the lesion.
- The size and shape of the lesion.
- The presence of calcification/septa/internal nodules.
- The wall/thickness of wall/sharpness of contour
- Homogenous/heterogenous.
- Presence/absence of enhancement.
- Pattern of enhancement in arterial, portal venous, and delayed phases.
- Potency of vessels.
- Surrounding hepatic parenchyma.
- Other specific features.

Follow-up of all patients was done either with biopsy, aspiration, surgical correlation, follow-up ultrasonography to look for the stability of the lesion, or additional investigations like MRI/nuclear scintigraphy. The final diagnosis was made. Then, results obtained were compared with the multiphasic contrast-enhanced helical CT imaging findings and tabulated.

RESULTS

The present study was carried out in the Department of Radiodiagnosis, Bhopal Medical Centre, Bhopal, Madhya Pradesh.

A total of 100 patients were included which were referred to our department with a history of focal liver lesions. Contrast-enhanced multiphasic CT was performed and evaluated for the underlying focal liver lesion.

In our study, majority of patients belonged to the age group 30–39 years (29%) and males constituting 55% of cases. The most common clinical presentation was that of pain in abdomen seen in 57% of cases. The second most common presentation was that of the history of malignancy elsewhere seen in 36%.

The right lobe alone was involved in the majority of patients (40%) followed by bilateral lobe involvement in 39%. The majority of patients were found to have multiple lesions seen in 51% of cases.

In our study, the majority of cases diagnosed were that of malignant lesions in 47% of cases. The other lesions diagnosed were benign lesions in 34% of cases and inflammatory lesions in 19% of the cases.

Among the benign lesions, the most common diagnosis in our study was simple cyst seen in 53% of cases. The second most common diagnosis was that of hemangiomas seen in 35% of cases.

Among the malignant lesions, the most common diagnosis was that of metastases seen in 67% of cases. The next most common was hepatocellular carcinoma (HCC) seen in 29% of cases.

Among the inflammatory lesions, the most common diagnosis with liver abscess was seen in 58% of cases followed by hydatid cyst seen in 42% of cases [Table 1-4].

DISCUSSION

Table 1: Etiological distribution of cases

Type of lesions	Number of cases (%)
Benign	34 (34)
Malignant	47 (47)
Inflammatory	19 (19)
Total	100 (100)

Table 2: Distribution of benign lesions

Type of lesion	Number of cases (%)
Simple cyst	18 (53)
Hemangiomas	12 (35)
Focal nodular hyperplasia	1 (3)
Focal fat	2 (6)
IHE	1 (3)
Total	34 (100)

Table 3: Distribution of malignant lesions

Lesion	Number of cases (%)
HCC	14 (29)
Cholangiocarcinoma	1 (2)
Hepatoblastoma	1 (2)
Metastases	31 (67)
Total	47 (100)

HCC: Hepatocellular carcinoma

Table 4: Distribution of inflammatory lesions

Lesion	Number of cases (%)
Livers abscess	11 (58)
Hydatid cyst	8 (42)
Total	19 (100)

Contrast-enhanced multiphasic CT plays an indispensable role in the detection and characterization of focal lesions of the liver. The aspects of the identified liver abnormalities influence the clinical and surgical decision-making. Benign abnormalities such as cysts and hemangioma do not require treatment, but some benign cases require treatment such as FNH and hepatocellular adenoma requires treatment in some cases. Malignant lesions arising from the liver such as HCC often need treatment. Metastases may or may not be amenable to treatment.

In our study, majority of the patients were presented with unilateral involvement of the right lobe only in 40% of cases. This was followed by bilateral lobar involvement seen in 39% of cases. This is in concordance with the distribution of focal liver lesions more common on the right lobe as seen in the observations by Joseph *et al.*,^[4] John *et al.*,^[5] and Kamel *et al.*^[11]

Among solid lesions, the most common enhancement pattern was that of hypo-hypo-hypo pattern seen in 34% of cases. This is due to the increased number of metastases cases. This is followed by the hyper-A-A pattern seen in 24.5% and arterial-arterial-arterial pattern in 19% of cases. This is similar in the incidence to the study conducted by van Leeuwen *et al.*^[6] Other patterns of enhancement were seen in the lesser frequency of cases.

Hemangiomas were diagnosed by the presence of a hypodense lesion with peripheral nodular enhancement of arterial attenuation with centripetal fill in van Leeuwen *et al.*^[6] and Murcio *et al.*^[7] One case of hemangioma was wrongly diagnosed as HCC (false negative) due to the presence of a Hyper-A-A pattern of enhancement.

FNH was diagnosed as a hypo/isodense lesion with homogenous arterial enhancement and a hypodense central cleft corresponding to the scar Joseph *et al.*^[4] and van Leeuwen *et al.*^[6] One case was wrongly diagnosed as metastases (false negative), and it had Hyper-A-A pattern.

Focal fat was diagnosed by the presence of a hypo-hypo-hypo lesion showing no enhancement, located adjacent to the falciform ligament and without any mass effect.

HCC was diagnosed by the presence of a heterogenous hypodense mass with hyperenhancement in the arterial phase with or without abnormal internal vessels and washout in venous phase Fernandez *et al.*^[8] One case of regenerative nodule in cirrhotic liver and a case of hemangioma were wrongly diagnosed as HCC (false positive).

Cholangiocarcinoma was diagnosed by the presence of a hypodense ill-defined lesion with delayed and prolonged enhancement Evelyn *et al.*^[9]

1HE was identified by the presence of solitary/multiple hypodense lesions with arterial enhancement becoming isodense in the delayed phase.^[10] One case was seen and diagnosed correctly using these criteria. Multiple lesions were seen distributed throughout the liver. Associated cutaneous hemangiomas were also seen.

Hepatoblastoma was diagnosed by the presence of a large hypodense lesion with calcification and mixed pattern of enhancement. 55% of cases showed calcification in a study of 50 cases by Abraham *et al.*^[10]

Metastases were diagnosed by the presence of variable density lesions, variable enhancement patterns, and necrosis and h/o malignancy in the patient. Metastases constituted the majority of diagnosis in our study comprising 31% of the overall diagnosis. The most common primary was from colorectal carcinoma (7 cases) followed by metastases from GB (6 cases). The most common enhancement pattern was hypo-hypo-hypo pattern seen in 65% of cases followed by hyper (rim)-hypo-hypo in 17% and mixed-mixed-mixed pattern in 11% of cases. This is similar to the study done by van Leeuwen *et al.*^[6] where hypo-hypo-hypo pattern was most commonly seen in 50% of cases.

Among 31 diagnoses of metastases, 29 were true positives and 2 were false positives. One of the lesions with hypo-hypo-hypo pattern with necrosis on follow-up turned out to be granulomatous (tubercular) lesion. The appearance of this is non-specific and may mimic metastases.^[11] Another lesion in a patient with seminoma with hyper-A-A pattern on follow-up turned out to be FNH which was missed due to the absence of the hypodense scar.

CONCLUSION

The accuracy of contrast-enhanced multiphasic CT in detecting and characterizing focal liver lesions is high, and it should be considered in the imaging workup of any patient with focal liver lesions. This helps in guiding further management of these patients avoiding unnecessary investigations and workup for the diagnosis as there is a high incidence of benign pathologies in the liver.

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Nasal Retrograde Intubation in Oromaxillofacial Surgery Patients with Limited Mouth Opening: A Cross-sectional Study

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Abstract

Introduction: Retrograde intubation is an alternative technique of securing definitive airway in the patients with limited mouth opening (LMO) when blind nasal intubation fails, and fiber-optic bronchoscope is unavailable. Retrograde intubation in patients with LMO <2 cm through nasal route is an alternative method for airway management.

Materials and Methods: The procedure was performed on 36 patients requiring maxillofacial surgical procedures to increase mouth opening. Indication for this technique was oral mucous fibrosis (OSMF; $n = 12$), temporomandibular joint (TMJ) ankylosis ($n = 8$), mandibular fracture ($n = 12$), and derangement of TMJ ($n = 4$). All patients were examined for pre-operative interincisal opening; during intubation through specific parameters and also post-operative findings were observed.

Results: The mean time was 5.6 min in successfully intubated patients. Eight patients had sore throat which resolved in few days and two patients had subcutaneous emphysema managed conservatively. No other complications were detected.

Conclusion: Retrograde nasotracheal intubation is an effective and useful technique for airway management in LMO patients with minimal risk.

Key words: Intubation, Limited mouth opening, Maxillofacial surgery, Nasotracheal retrograde intubation

INTRODUCTION

Patients with limited mouth opening (LMO) conditions increase the difficulty in securing the airway.^[1-3] Maxillofacial surgical patients present with specific challenge for the surgeon and anesthetist. Blind nasal intubation remains an important auxiliary subsidizing airway in such patients when fiber-optic bronchoscope is not available.^[4-6] The key in these situations is to perform an elective short-term tracheostomy before the operation which carries high incidence of complications.^[7] Other methods are to insert the tracheal tube to submental or submandibular approach;^[8,9] however,

it can be preposterous in temporomandibular joint (TMJ) ankylosis and is associated with complications such as skin infection, salivary gland damage, nerve damage, and formation of scar. Nasal route intubation is more favorable as these patients require surgical procedures either intraoral, extraoral, or both.^[10] Retrograde nasotracheal intubation is an effective and useful technique for airway management in LMO patients <2 cm.

MATERIALS AND METHODS

The study was performed on 36 patients with LMO posted for elective surgery under general anesthesia at the department of ENT head neck surgery. Patients who underwent awake retrograde nasotracheal intubation under regional airway anesthesia were included in the study. Inclusion criteria in the study were as follows: (a) Patients with LMO <2 cm and (b) nasal intubation suitable for surgical procedure. TMJ ankylosis patients who had failed 3 times blind nasal intubation underwent retrograde

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intubation were also included in the study. Exclusion criteria were as follows: (a) Patients required more invasive and surgical techniques for securing the airway, (b) significantly deviated nasal septum and previous nasal surgery, (c) local infection in nose or pathological abnormalities of airway, and (d) oral intubation was suitable for surgical procedures. The institutional ethics committee approved the protocol. After detail discussion and written informed consents were obtained from each patient for retrograde nasotracheal intubation.

The pre-operative medical assessment included routine surgical profile, electrocardiogram, and chest X-ray followed by pre-anesthetic evaluation. From each patient, previous history of surgeries under general anesthesia, difficulty in intubation and complication during surgery was asked and noted.

Patients were told about the need of awake nasotracheal intubation, its complications the type of airway anesthesia and need of any airway intervention in emergency. After detail explanation about the technique, questions were answered. The active participation of the patients in the process of intubation was asked. The patients were informed of what he/she has to do, to assist in smooth intubation. For example, taking deep breaths, maintaining the head position, and swallowing secretion as and when required. On the night before surgery, pantoprazole 40 mg and metoclopramide 5 mg orally were given to prevent acid reflux and aspiration. Patients were kept nil by mouth 6 h before surgery. On the morning of surgery, intravenous access was secure and premedication was given 1 h before the procedure which includes injection amoxicillin with clavulanic acid 1.2 g, injection metronidazole 100 mL, 500 mg (antibiotic), injection dexamethasone 8 mg (steroid), injection ondansetron 4 mg (antiemetic), injection pantoprazole 40 mg (antacid), injection glycopyrrolate 0.2 mg (antisialagogue), and a nasal decongestant (xylometazoline 2%). The patient was then asked to gargle and swish around 10 mL of lignocaine viscous 4% without swallowing. Bilateral superior laryngeal nerve block and transtracheal injection of the local anesthetic were given.^[11,12] Cook retrograde intubation set (Cook Medical, Bloomington, IN, USA) was used. The procedure was performed as described by David Burbulys and Kianusch Kiai.^[13] The technique proceed by an initial percutaneous puncture through the cricothyroid membrane made with the introducer needle and catheter at a 30–40° angle to the skin in a cephalad direction. The free flow of air bubbles in the syringe confirms entry into the trachea. Holding the catheter in place, the needle and syringe are removed [Figure 1]. The J-tip of the wire was passed up the trachea until it retrieved from the nose with fingers [Figure 1]. A black proximal positioning mark on the wire should be visible at the skin access site, ensuring that enough was exposed nasally to

facilitate the subsequent passage of the guiding catheter (custom made guide by Cook) and endotracheal tube from the other end. The catheter sheath at the skin was removed, and the wire is clamped at this site to stabilize its entry into the skin at the cricothyroid membrane. The guiding catheter was advanced antegrade over the wire, by way of the nose, into the trachea until tenting is noted at the cricothyroid access site [Figure 2]. The needle holder was unclamped, and the wire was removed to prevent damage to cricothyroid membrane. The flexometallic endotracheal tube was then passed (railroaded) over guiding catheter into position below the level of the vocal cords [Figure 3] and guiding catheter was removed, as the endotracheal tube was further advanced into final position. Later, tracheal tube position was confirmed by observing the movements of

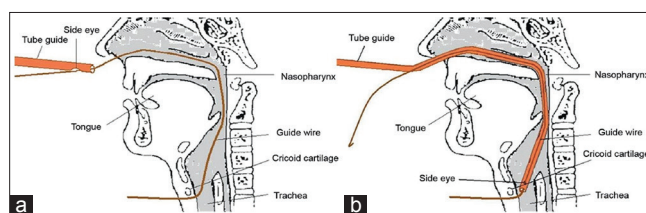


Figure 1: (a and b) An initial percutaneous puncture through the cricothyroid membrane and J-tip of the wire was passed up the trachea until it retrieved from the nose

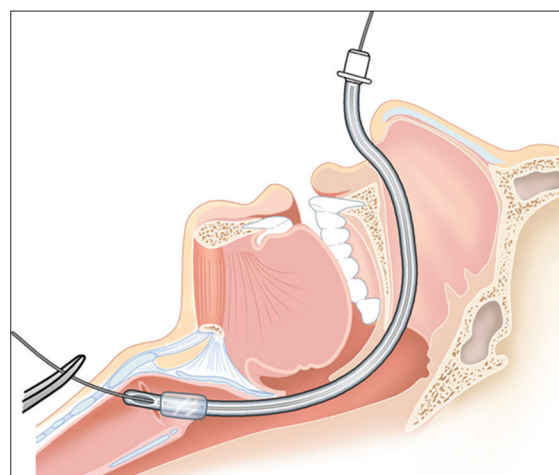


Figure 2: Guiding catheter advanced antegrade over the wire

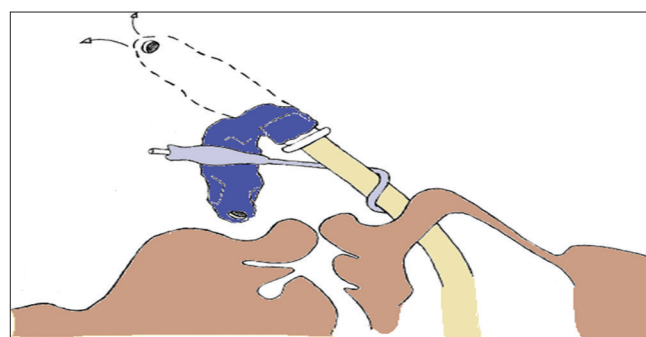


Figure 3: Flexometallic endotracheal tube passed (railroaded) over guiding catheter

reservoir bag of breathing circuit, capnography, and pulse oximeter. The balloon cuff was inflated, and tube was taped and secured. Endotracheal tube was connected to Boyle's machine and induction of anesthetic drugs done as usual fashion.

Size of endotracheal tube, nare intubated (right or left), exchange from one nare to another, number of attempts, time taken for successful intubation, tip of wire manipulation - manipulation of the tip of the instrument to obtain successful intubation (include 1. Not difficult - on initial introduction, little or no manipulation of the wire was needed, 2. Moderately difficult - moderate manipulation of the wire needed, and 3. Difficult - extensive manipulation of the wire including correction of wire to bring it out of nose and often with changes in position of the operator), patient comfort (Grade I - no movement observed, Grade II - coughing observed, Grade III - extremity movement observed, and Grade IV - violent movement observed), surgeon and anesthetist's comfort and time saving (no surgical intervention needed to intubate the patient), post-operative complications (nose pain, neck pain, and sore throat), and patient satisfaction (excellent, good, and fair) were noted.

RESULTS

A total of 36 patients (n) were enrolled over a study over a period of 2 years and fulfilled the inclusion criteria. Retrograde intubation was performed successfully on 28 males (77.8%) and 8 females (22.2%). Mean (SD) interincisal distance 11.7 (6.56) mm is shown in Table 1. All female patients (n = 8; 22.2%) were intubated with endotracheal tube size 7, compare to male patients (n = 28; 77.8%) intubated with 7.5. 28 patients (77.8%) were successfully intubated in the first attempt, whereas 6 patients (16.7%) underwent intubation in the second attempt and 2 patients (5.5%) underwent intubation in the third attempt, respectively.

Overall, mean time taken from puncture of cricothyroid membrane till confirmation of intubation was 5.6 (1.66) min. Most of the patients (n = 18; 50%) had no difficulty in manipulation of tip and showed Grade I patient comfort which was mostly seen in patients with mandibular fracture (n = 12) and OSMF (n = 6). However, 27.8% (n = 10) and 22.2% (n = 8) patients showed moderate difficulty and difficulty in manipulation of tip, respectively.

Grade II (n = 6; 16.7%) and Grade III (n = 4; 11.1%) patient comfort was seen among patients with OSMF and internal derangement of TMJ, respectively. Grade IV patient comfort with difficult tip manipulation was observed in patients with TMJ ankylosis (n = 8; 22.2%).

Patients with internal derangement of TMJ had Grade III patient comforts. No major complications occurred to our patients except for minor bleeding from the nose and puncture site which stopped spontaneously. However, one patient with OSMF had surgical subcutaneous emphysema which was conservatively managed and resolved spontaneously [Table 2].

Table 1: Patient characteristics

Patient characteristics	n (%)	Mean (SD)
Overall mean age (years)		31.78 (7.27)
21–30	18 (50)	25.78 (2.48)
31–40	12 (33)	34.67 (1.96)
41–50	06 (16.7)	44 (2)
Sex		
Male	28 (77.8)	
Female	8 (22.2)	
Indication for retrograde intubation		
Mandibular fracture	12 (33.3)	
OSMF	12 (33.3)	
TMJ ankylosis	8 (22.2)	
Internal derangement of TMJ	4 (11.1)	
Interincisal distance (mm)		11.7 (6.56)
Site of surgery		
Mandible	12 (66.7)	
Buccal mucosa	6 (33.3)	

SD: Standard deviation

Table 2: Observations during intubation

During intubation	n (%)	Mean (SD)
Size of endotracheal tube		
7	8 (22.2)	
7.5	28 (77.8)	
Nare intubated		
Right	8 (22.2)	
Left	28 (77.8)	
Exchange from one nare to another	6 (16.7)	
Number of attempts		
1 st	28 (77.8)	
2 nd	06 (16.7)	
3 rd	02 (5.5)	
Overall, mean time of successful intubation (min)		
Mean time of successful intubation for following indications (min)		5.6 (1.66)
Mandibular fracture		6.01 (1.50)
OSMF		4.42 (0.30)
TMJ ankylosis		6.66 (1.75)
Internal derangement of TMJ		5.95 (3.48)
Tip manipulation		
No difficulty	18 (50)	
Moderate difficulty	10 (27.8)	
Difficult	08 (22.2)	
Patient comfort		
Grade I	18 (50)	
Grade II	06 (16.7)	
Grade III	04 (11.1)	
Grade IV	08 (22.2)	
Surgical subcutaneous emphysema	02 (5)	
Surgeon's and anesthetist comfort	36 (100)	
Surgeon's and anesthetist time saving	36 (100)	

SD: Standard deviation

During post-operative period, 32 patients complained of nose pain and 28 patients pain near cricothyroid membrane puncture near anterior neck region which was resolved gradually as all patients were under intravenous antibiotics and intramuscular analgesics for 3 days. Four patients had sore throat which subsequently resolved in few days. Patient satisfaction was excellent in 18 patients (50%) and 33.3% good in 12 patients. TMJ ankylosis patients who had Grade IV patient comfort showed fair satisfaction ($n = 6$, 16.7%), but two patients had good satisfaction [Table 3].

DISCUSSION

Several modifications ^[2,7,13-17] of this technique have been made since its introduction for almost 55 years ago by Butler and Cirillo,^[18] to secure difficult airways in both elective and emergency cases resulting in fewer complications. In the present study, J-shaped wire was removed before the insertion of endotracheal tube through guiding catheter which minimized trauma associated with wire at the cricothyroid site. At the same time, guiding catheter should be held in position firmly to prevent accidental dislodgement of tip of endotracheal tube into the esophagus, and guiding catheter is removed slowly as endotracheal tube is advanced into final position in the trachea. Pressure applied should be normal as overzealous pressure of the tube may lead to folding.^[19] The interesting finding of this study not reported earlier was that patients ($n = 28$, 77.8%) had increased incidence of intubation through the left nare [Figure 1]; probably, because it depends on the exit of wire and is beyond the anesthetist control.

Barriot and Riou^[20] reported retrograde technique in 19 patients with either maxillofacial trauma or cervical spine injury and found all were intubated successfully within 5 min on only one attempt. In the present study, most of the patients succeeded on the first attempt ($n = 28$, 77.8%) with Grade I patient comfort due to no difficulty in tip manipulation and mean time taken to intubate all patients was 5.6 min. However, patients who had more than one attempt took more time (6.66 min) to intubate were with TMJ ankylosis ($n = 8$; 22.2%) and had Grade IV patient comfort due to difficult tip manipulation. They had distorted anatomy of airway^[21] with severe restriction

in mouth opening, microgenia and had failed attempts of blind nasal intubation, which could be the possible reason. Similar finding was reported by Bhattacharya *et al.*^[2] in two patients with TMJ ankylosis requiring gap arthroplasty but used a suction catheter to retrieve an epidural catheter from the pharyngeal cavity, which had been passed retrogradely from a cricothyroid puncture to aid intubation successfully in their patients. To have Grade I patient comfort, regional anesthesia of the airway should also be effective.^[11] In patients with TMJ ankylosis due to deformed airway anatomy, achieving profound regional airway anesthesia may be difficult. However, patients who had moderate difficulty in tip manipulation and Grades II and III patient comfort were because as tracheal tube impinges against the larynx during retrograde intubation and multiple attempts may be required to negotiate it into the trachea as stated by Shantha.^[16]

In retrograde intubation technique, there are two parts: “Guidance” consists of retrograde insertion of a catheter from the larynx to the mouth or nose, and the “blind” part is the insertion of endotracheal tube into trachea without visualization of vocal cords. Hence, it is perhaps better described as guided blind intubation or translaryngeal intubation.^[7] We present OSMF and internal derangement of TMJ as new indications of retrograde intubation than those wide range of other indications reviewed by Dhara^[7] previously. Furthermore, we used in mandibular trauma and TMJ ankylosis.

In the present study, Cook retrograde intubation set was used successfully with no complications except for one patient who had surgical subcutaneous emphysema which was conservatively managed and resolved spontaneously. Furthermore, minor bleeding was noticed at the puncture site during intubation. Each technique has some complaints from the patient side. Postoperatively, patients complained of nose pain, pain near anterior neck region, and sore throat that was resolved gradually. We encountered no such major complications. The main advantages of retrograde technique as observed in this study were as follows: Simple and useful technique in LMO patients, especially when blind nasal intubation fails and expensive equipment fibroscope is not available,^[2,7] minimal requirement of equipment, and laryngeal inlet does not have to be identified or negotiated^[7] and can be performed safely in experienced hands without any complications.^[7,13] In patients with LMO retrieval of the guide and achieving retrograde nasotracheal intubation can be challenging.^[7]

In the present study, the technique was successfully used in 36 patients with LMO <2 cm undergoing oral and maxillofacial surgery. It was found that most patients had excellent satisfaction and add no complications of its

Table 3: Post-operative findings

Post-operative findings	n (%)
Nose pain	16 (88.69)
Sore throat	4 (22.2)
Pain near cricothyroid puncture	14 (77.8)
Patient satisfaction	
Excellent	9 (50)
Good	6 (33.3)
Fair	3 (16.7)

own. In conclusion, retrograde nasotracheal intubation is a convenient, effective, and useful technique for airway control in patients with LMO and with only a small risk potential.

Many retrograde and antero-grade guides have been reviewed by Dhara.^[7] Many studies^[22-25] described new approaches to retrograde intubation. Unfortunately, some mouth opening is essential to use these approaches. If absolutely no mouth opening is present, a pharyngeal catheter may be used.^[2]

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Comparison between Two Regimens of Art in Human Immunodeficiency Virus Patients at Tertiary Care Art Centre Jabalpur: A Prospective Observational Study

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Abstract

Objective: The objective of the study was to assess the effectiveness of two regimens (Tenofovir + Lamivudine + Efavirenz [TLE] and Zidovudine + Lamivudine + Nevirapine [ZLN]) on the basis of CD₄ count changes among human immunodeficiency virus (HIV) patients along with occurrence of adverse drug reactions (ADRs) by these regimens.

Materials and Methods: A prospective observational study with a sample size of 200, divided equally into two groups of 100 each jointly conducted in the Tertiary Care ART Centre Jabalpur, from April 2016 to June 2017. Group A contains TLE regimen, and Group B contains ZLN regimen. Various ADRs were observed in both the groups.

Results: Most of the patients were male (124) in our study with a maximum incidence of HIV found among 21–40 years of age group. The average increase in the CD₄ count was significant only in Group A (<0.05). 83% and 93% patients of Groups A and B, show a total of 137 and 165 ADRs, respectively. Group A shows major central nervous system and gastrointestinal tract and Group B shows mainly dermatology and hematological type of ADRs. Using Modified Hartwig and Siegel severity assessment scale, we found that in Group A, ADR was mild to moderate in nature while in Group B, ADR was mainly moderate in nature.

Conclusion: It was concluded that Group A containing TLE regimen was more effective as their CD₄ count was significantly increase after a follow-up of 6-month treatment with least ADR and the patients who develop ADR was mainly mild in nature.

Key words: Adverse drug reaction, CD₄ count, Tenofovir + Lamivudine + Efavirenz, Zidovudine + Lamivudine + Nevirapine

INTRODUCTION

Human immunodeficiency virus infection/Acquired immunodeficiency syndrome (HIV/AIDS) is a disease of the human immune system caused by the HIV.^[1] The HIV, a lentivirus (subgroup of retrovirus), infects cells (specifically the CD₄ cells/helper T cells, a type of white blood cell) of the immune system, destroying or impairing their function. Infection with the virus results

in progressive deterioration of the immune system, leading to “immune deficiency.” Infections associated with severe immunodeficiency are known as “opportunistic infections,” because they take advantage of a weakened immune system. Acquired immunodeficiency syndrome (AIDS) is a term which applies to the most advanced stages of HIV infection. It is defined by the occurrence of any one among more than 20 opportunistic infections or HIV-related cancers.

Virus can be transmitted through unprotected sexual intercourse with an infected person, transfusion of contaminated blood, and the sharing of contaminated needles, syringes, surgical equipment, or other sharp instruments. It may also be transmitted between a mother and her fetus during pregnancy, childbirth, and while breastfeeding.^[2]

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AIDS is a global problem. It has been reported from more than 190 countries around the world and a pool of HIV infected persons in Africa and Asia is large and expanding.^[3]

In India, approximately 2.1 million people are living with HIV in 2016, which is estimated to be the third largest population of HIV affected people in the world. In 2016, HIV prevalence in India was estimated to 0.3% and 62,000 people died from AIDS-related illnesses. Estimated numbers of new HIV infections in 2016 were 80 thousand and 1 million people are on ART who are living with HIV. The number of people newly initiating ART in 2016 was 176969.^[4]

The world has committed to end the AIDS epidemic by 2030. UNAIDS recommends a Fast-Track approach to achieve the 90–90–90 treatment target by 2020, whereby 90% of people living with HIV should know their HIV status, 90% of people who know their HIV-positive status are accessing treatment and 90% of people on treatment have suppressed viral loads. Global consensus and leadership have driven greater investment of financial and human capital, and mounting clinical experience and research, improved treatment regimens and diagnostics, and reductions in the price of medicines have created gains in efficiency and effectiveness.^[5]

Antiretroviral therapy (ART) became the keystone of National AIDS programme. With the advent of new antiretroviral drugs, there has been decline in morbidity and mortality due to AIDS.^[6] Most of the drugs which are available and approved for use in highly active ART have some of the other adverse effects; thus, the treatment of HIV infection has become a complicated balancing acts between the benefits of durable HIV suppression and the risks of drug toxicity.^[7]

This study was to assess the effectiveness of two regimens (Tenofovir + Lamivudine + Efavirenz [TLE] and Zidovudine + Lamivudine + Nevirapine [ZLN]) on the basis of CD₄ count changes among HIV patients along with occurrence of adverse drug reactions (ADRs) by these regimens.

MATERIALS AND METHODS

It was an observational study and was conducted on 200 HIV patients for the duration of 15 months from April 2016 to June 2017 in Tertiary Care ART Centre Jabalpur. The cases were selected on the basis of inclusion criteria, i.e., age >20 years and take well-informed consent from all participants. The patients who were switch to other therapy due to intolerance were excluded from the study. Details of the participants were kept confidential.

All participants were divided into two groups 100 each.

Group A ($n = 100$) (TLE regimen)

Group B ($n = 100$) (ZLN regimen)

Suitably structured pro forma was used to assess the details of the patients, family history, and duration since HIV diagnosed. Baseline CD₄ count, type of regimen and essential laboratory investigations such as complete blood counts, liver function tests, renal function tests, lipid profile, blood sugar tests, and chest X-ray (P-A view) was also done. The recent CD₄ counts and other investigations of all participants were done during follow-up of 6-month period as the patients usually visited at 6 months for their CD₄ count. Any associated ADR was also noticed during therapy and assessed for their severity using Modified Hartwig and Siegel scale.^[8]

Tools in the Study

Modified Hartwig and Siegel scale.^[8]

Hartwig *et al.* categorized ADRs into seven levels as per their severity level 1 and 2 fall under mild category, level 3 and 4 under moderate, and level 5, 6, and 7 fall under category severe.

Mild

Level 1: An ADR occurred but required no change in treatment with the suspected drug.

Level 2: The ADR required that treatment with the suspected drug be withheld, discontinued, or otherwise changed. No antidote or other treatment requirement was required. No increase in length of stay.

Moderate

Level 3: The ADR required that treatment with the suspected drug be withheld, discontinued, or otherwise changed.

AND/OR

An antidote or other treatment was required. No increase in the length of stay.

Level 4: Any level 3 ADR which increases length of stay by at least 1 day.

OR

The ADR was the reason for the admission.

Severe

Level 5: Any level 4 ADR which requires intensive medical care.

Level 6: The adverse reaction causing permanent harm to the patient.

Level 7: The adverse reaction either directly or indirectly led to the death of the patient.

Statistical Analysis

The data were analyzed using SPSS 20. Appropriate method was used during analyzing such as mean, standard deviation (SD), Chi-square test, and Paired *t*-test.

RESULTS

Most of the patients were male (124) in our study [Table 1 and Figure 1]. Maximum incidence of HIV was found among 21–40 years of age group (80%) followed by 41–60 years of age group (20%). The mean age \pm SD was 34.08 ± 9.21 years [Table 2 and Figure 2]. These demographic data were not statistically significant.

The average increase in the CD4 count was significant only in Group A (<0.05) [Table 3]. 83% and 93% patients of Groups A and B show a total of 137 and 165 ADRs, respectively [Table 4 and Figure 3].

Table 5 and Figure 4 show the system involved in ADR. In Group A major central nervous system (CNS) and gastrointestinal tract (GIT) system were involved and in Group B major system involved was dermatology and hematology. Table 6 and Figure 5 show severity assessment of ADR in patients using Modified Hartwig and Siegel severity assessment scale and found that in Group A, ADR was mild to moderate in nature while in Group B, ADR was moderate in nature.

DISCUSSION

This is an observational study, with the male predominance in both the groups. The maximum patients were belongs to 21–40 age with the mean \pm SD of 34.08 ± 9.21 years. This is concordance with the study of Sehgal *et al.*^[9] The immunological response is measured by CD4 count. It was seem that **Group A** who receive TLE regimen, average raise of CD4 count after the follow-up of 6 months, was 189.51 ± 234.95 SD of mean value, which was statistically significant ($P < 0.05$) than Group B who receive ZLN regimen where average raise of CD4 count was 191.82 ± 191.48 which was statistically not significant ($P > 0.05$). It seems that patients, who were on TLE therapy, were effectively increased in their CD4 count compared to ZLN therapy. Our study was accordance with the Rajput *et al.*^[10] study who also found that the TLE regimen was effective than ZLN in term of CD4 count. Another study by Krishnan *et al.*^[11] also found similar observation in their study. The incidence of ADR in Group A was 83% and in Group B was 93% with the total of 137 and 195 ADR in both the groups, respectively. Group A found maximum of CNS- (49.6%) and GIT (22.6%)-related ADRs. CNS

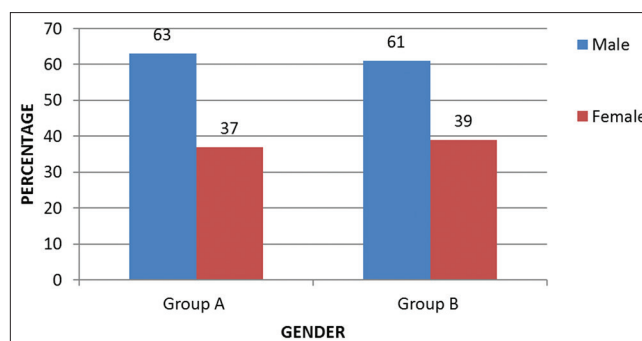


Figure 1: Gender distribution

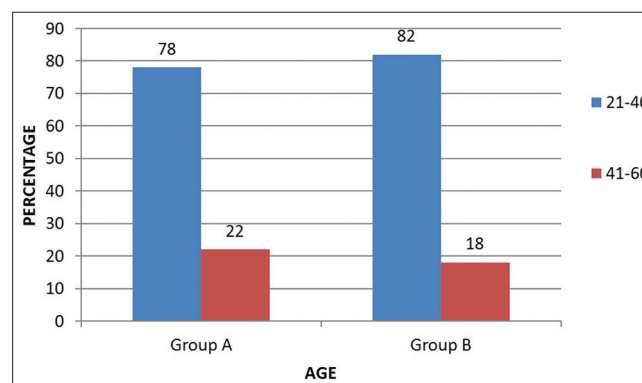


Figure 2: Age distribution

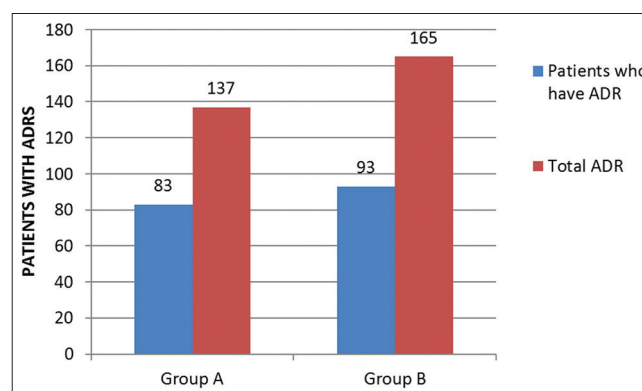


Figure 3: Patient found adverse drug reaction in both the groups

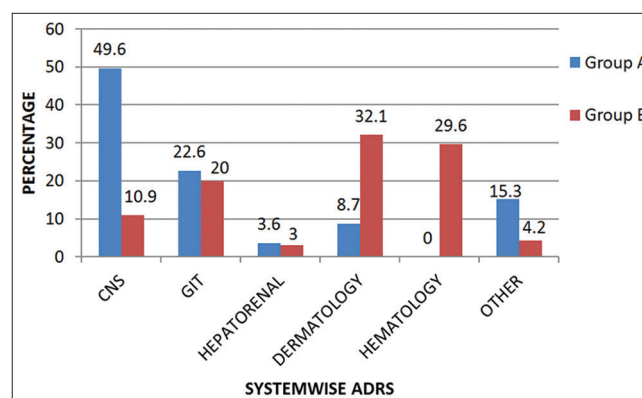


Figure 4: System involved in adverse drug reaction

Table 1: Gender distribution

Gender	Group A (n=100)	Group B (n=100)	Total
Male	63	61	124
Female	37	39	76

$\chi^2=0.084$; $P>0.05$ at 1 df

Table 2: Age distribution

Age	Group A (n=100)	Group B (n=100)	Total
21–40	78	82	160
41–60	22	18	40
Mean±SD	34.34±9.85	33.83±8.56	34.08±9.21

$t=0.70$; $P>0.05$. SD: Standard deviation

Table 3: CD4 count before and after the therapy

Regimen group	Baseline CD4 count (cell/μL)	CD4 count after 6 month (cell/μL)	Average increase in CD4 count	P value
Group A	272.6±190.25	462.11±220.84	189.51±234.95	0.0046
Group B	275.6±204.66	467.42±201.38	191.82±191.48	0.3022

Table 4: Patient found ADR in both the groups

Parameter	Group A (n=100)	Group B (n=100)
Patients who have ADR	83	93
Total ADR	137	165

ADR: Adverse drug reaction

related ADR were mainly dizziness, headache, neuropathy and psychosis and GIT associated ADR were mainly nausea and gastritis. Similar finding was also observed by Jain *et al.*^[12] where they found that majority of ADR were related to CNS (40.3%) followed by GIT (37.5%). Lorio *et al.*^[13] studied too endorsed with our study who found that 45.5% of ADRs were pertaining to CNS, 27.3% to gastrointestinal system. Group B found dermatological (32.1%), i.e., rashes and itching, and hematological (29.6%), i.e., anemia and neutropenia as the most common ADRs. Sharma *et al.*^[14] observed cutaneous ADR (44.4%) as the most common ADR followed by hematological (32.2%) in their study.

In Group A, maximum ADR was mild to moderate in nature, and only 6 patients have develop severe in nature compare to Group B where the majority of ADR was moderate in nature, and only 8 patients develop a severe reaction, using Modified Hartwig and Siegel severity assessment scale. Similar type of results was found by Anwikar *et al.*^[15] where 8.77%, 77%, and 14.02% ADRs were mild, moderate, and severe, respectively.

CONCLUSION

It was concluded that both the regimen were effective in the treatment of HIV. In term of the CD4 count after

Table 5: System involved in ADR

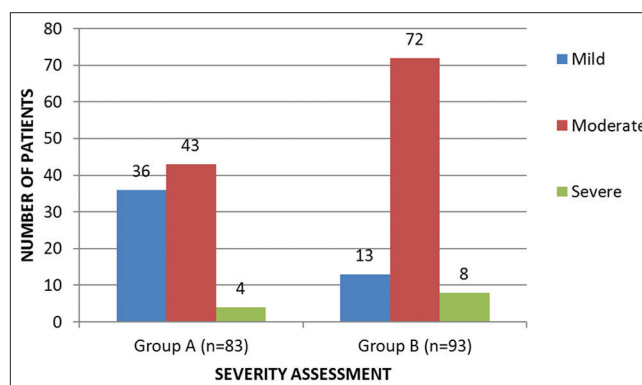
System involved	Group A n=137 (%)	Group B n=165 (%)
CNS	68 (49.6)	18 (10.9)
GIT	31 (22.6)	33 (20)
Hepatorenal	5 (3.6)	5 (3)
Dermatology	12 (8.7)	53 (32.1)
Hematology	0 (0)	49 (29.6)
Other	21 (15.3)	7 (4.2)

CNS: Central nervous system, GIT: Gastrointestinal tract

Table 6: Severity assessment (modified Hartwig and Siegel severity assessment scale)

Severity of ADR in patients	Group A (n=83)	Group B (n=93)
Mild	36	13
Moderate	43	72
Severe	4	8

ADR: Adverse drug reaction

**Figure 5: Severity assessment**

follow-up of 6 months, the TLE regime shows the better outcome with least ADR. The patients who develop ADR were mild in nature and subsided spontaneously after few weeks without switch off the therapy or either managed by counselling and or symptomatic treatment.

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Serum Albumin and Uric Acid Estimation in Ischemic Heart Disease Patients

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Abstract

Aim: The aim of the study was to evaluate serum uric acid and serum albumin levels in ischemic heart disease patients (IHD).

Materials and Methods: Around 60 persons were recruited for the study, with 30 patients diagnosed as IHD and 30 healthy volunteers. Serum uric acid and serum albumin were estimated using Semi Auto Analyzer. Statistical analysis was performed using SPSS version 16. The parameters were compared among two groups using independent *t*-test.

Results: Serum uric acid levels ($P = 0.000$) were increased significantly in Group II patients compared to those in Group I controls. There was no significant difference in serum albumin levels among the two groups. Levels of serum albumin in Group I and Group II are almost similar.

Conclusion: From this study, serum uric acid can be used to assess the prognosis of patients with IHD. Our study showed a normal serum albumin levels in both the groups, but low serum albumin is associated with high mortality in general.

Clinical significance: Recent studies have provided evidence that uric acid may play a role in the progression of various diseases including cardiovascular complications. As a result, the measurement of uric acid concentrations is now mandatory for the management of those disease states. Low serum albumin level causes subclinical fluid overload in IHD patients leading to poor prognosis. Hence, further studies have to be carried out to assess the association of quality of life in IHD patients and serum albumin levels.

Key words: Hyperuricemia, Hypoalbuminemia, Ischemic heart disease, Oncotic pressure, Semi Auto Analyzer

INTRODUCTION

According to 2010 Global Burden of Disease Study, ischemic heart diseases (IHD) was the single largest cause of death out of the total number of deaths in the combined regions of Central, Eastern, and Western Europe followed by cerebrovascular diseases.^[1] Coronary heart disease is the major cause of death and disability in the developed countries.^[2]

Uric acid is the final oxidation product of purine catabolism. Despite the fact that uric acid is an antioxidant, its role

in the pathogenesis of IHD has been well established in related studies. A systematic review and meta-analysis of hyperuricemia and coronary heart disease revealed the role of hyperuricemia as a risk factor for cardiovascular diseases.^[3]

Hyperuricemia is defined as uric acid levels more than 6.5 mg/dl in males and more than 6 mg/dl in females. Hyperuricemia is associated with the generation of free radicals, endothelial dysfunction, progression of atherosclerosis, and thrombus formation. Uric acid is mainly responsible for the propagation of oxidative stress.^[4] Pro-inflammatory pathway activation is mediated by uric acid.^[5] The fact that uric acid as a risk factor for IHD remains a controversy. Various epidemiologic studies conducted in the past concluded uric acid as a marker of cardiovascular diseases^[3] while some may contradict the statement.^[6]

Serum albumin is the major plasma protein synthesized by the liver. Albumin mainly contributes about 70–80% of

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plasma oncotic pressure.^[7] Hypoalbuminemia is implicated in the development of pulmonary edema.^[8] Pulmonary edema results when either an increase in the pulmonary capillary pressure or fall in the colloid osmotic pressure.^[9] According to Starling's hypothesis, reduced plasma oncotic pressure due to hypoalbuminemia causes shift of fluid from intravascular to interstitial space facilitating the onset of cardiogenic pulmonary edema. Furthermore, albumin binds and transports free fatty acids and protects against lipid peroxidation. Fatty acids may serve several cell functions such as gene expression and intracellular signal transduction. Some fatty acids are precursors of eicosanoids.^[7,10]

Studies show that hypoalbuminemia is a predictor of cardiovascular morbidity and mortality.^[11] Etiology of hypoalbuminemia may be due to malnutrition, reduced albumin production by the liver due to congestion, hemodilution, inflammation, etc.^[12] In our study, we made an effort to identify the relationship between uric acid, albumin, and the IHD.

Aim and Objectives

The objectives are as follows:

- To evaluate the serum levels of uric acid in IHD patients.
- To estimate serum albumin levels in IHD patients.

MATERIALS AND METHODS

A case-control study was conducted with 60 individuals of both the sexes in the age group of 35–75 years. They are divided into 2 groups of 30 each. Patients with the history of chest pain diagnosed as IHD patients by the cardiologist formed the Group 2. Standard pro forma was used for history taking, examination, and investigation. Proper written informed consent was obtained from the study group. Ethical Committee Clearance was obtained from the institutional review board.

Exclusion Criteria

The following criteria were excluded from the study:

- Chronic kidney disease
- Gout
- Malignancy
- Heart failure.

Specimen Collection and Processing

From the controls and the patients, 5 ml of venous blood was collected in a clot activator tube. Blood was allowed to clot for 30 min and serum was separated after centrifugation.

Analysis

Serum was analyzed for uric acid and albumin. The analytes were assayed using special kits from ERBA diagnostics.

The analysis of serum was performed using Semi Auto Analyzer.

Uric Acid Measurement: Uricase Method

Uricase converts uric acid into allantoin and hydrogen peroxide. Enzyme peroxidase couples hydrogen peroxide with phenolic chromogen to form a red colored compound and its absorbance was determined at the wavelength of 510 nm.

Albumin Measurement: Bromocresol Green (BCG)

BCG forms a colored complex with serum albumin and its absorbance was measured at the wavelength of 510 nm.

Statistical Analysis

"Independent *t*-test" was applied for statistical analysis. The outcomes were presented as mean (standard deviation) and $P < 0.05$ was considered significant and the parameters were compared among two groups. The analysis was performed using SPSS version 16.

RESULTS

In our study, we measured the levels of serum uric acid and albumin among the IHD patients and compared with that of age sex-matched normal volunteers. We found a significant change in serum uric acid as mentioned by *P* value by 2 tailed student test as seen in Table 1. The mean uric acid level in IHD patients was found to be 6.25 ± 1.7 mg/dl whereas it was 4.61 ± 0.7 mg/dl in the control group. Serum uric level was found to be higher in the IHD patients group. In the estimation of serum albumin, we did not notice any significant difference among the 2 groups (*P* value 0.2). In IHD patients, the mean albumin level in serum was 3.63 ± 0.48 g/dl, and in the normal group, the mean albumin level was 3.76 ± 0.45 g/dl. We also noticed a small decrease in the albumin levels in the patient group.

DISCUSSION

In our study, we found a significant association in serum uric acid levels between the two groups. As we are aware about the consequences of having high uric acid levels in IHD patients from other studies, it is better to have a constant watch in such patients to reduce the mortality

Table 1: Mean and standard deviation of serum uric acid and albumin in controls and patients

Parameter	Group 1 (controls)	Group 2 (IHD patients)	Student <i>t</i> -test Sig (2 tailed) <i>P</i> value
Uric acid (mg/dl)	4.61 ± 0.7	6.25 ± 1.7	0.000*
Albumin (g/dl)	3.76 ± 0.45	3.63 ± 0.48	0.2

* $P < 0.05$ was considered significant. IHD: Ischemic heart disease

rate. Many epidemiological studies have shown a significant correlation between elevated uric acid levels and diseases such as hypertension, atherosclerosis, stroke, and heart failure. In patients with heart failure and cardiovascular disease, uric acid levels in serum are used to predict mortality.^[13,14] However, according to Framingham heart study, uric acid was not associated with the progression of cardiovascular diseases.^[15]

Several cohort studies identified an association of elevated serum uric acid levels with the prognosis of cardiovascular diseases.^[16] In other studies, serum uric acid was identified as negative prognostic factor in case of severe heart failure.^[17] In yet another study, the relationship was determined between elevated serum uric acid levels with progression of acute myocardial infarction.^[18]

Humans convert purines, namely adenosine and guanosine to uric acid. During the conversion of hypoxanthine to uric acid catalyzed by xanthine oxidase, reactive oxygen species are produced. Xanthine oxidase is involved in the pathogenesis of IHD, reperfusion injury, and heart failure. A constant balance occurs between production and excretion of uric acid. Hyperuricemia commonly results when there is any derangement in the mechanism.^[13]

From our study, we could not find any significant change in albumin levels among the two groups. Hypoalbuminemia can cause worsening of cardiovascular diseases hence estimation of albumin will help to monitor IHD patients. In the Cardiovascular Health Study conducted by Gerasimos,^[19] hypoalbuminemia can be used to predict the risk of HF among community-dwelling elderly people. Furthermore, in some studies, hypoalbuminemia is found to be associated in the development of pulmonary edema.^[20] Hypoalbuminemia in cardiovascular disease patients is associated with increased risk of mortality.^[21]

CONCLUSION

Our study demonstrated an elevated serum uric acid levels which are significantly higher in IHD patients when compared to normal individuals hence monitoring of serum uric acid could guide the outcome or prognosis in IHD patients. Serum albumin levels were not significantly elevated in this study. Since an increased risk of mortality is established in hypoalbuminemia patients, constant measurement of serum albumin levels will improve the outcome in IHD patients.

Limitations of the Study

The sample size is small and would have been better if it was a longitudinal study. The analytes of our study may be

affected by some diseases or treatment with some drugs. All the chronic diseases were not ruled out. Other markers of inflammation like C reactive proteins were not assessed in our study protocol.

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Trends in Breast Feeding Practices among Mothers at a Tertiary Care Institute

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Abstract

Introduction: Breastfeeding is a natural and traditional infant feeding practice throughout the world. Appropriate feeding is crucial for healthy growth and development. Hence, a study of infant feeding practice that is prevalent is essential to outline trends of feeding practices before the formulation of any need-based program.

Aims and Objectives: The objectives of the study were to study the knowledge, attitude, and practice regarding breastfeeding, its correlation with maternal factors and about the introduction of other milk and weaning foods.

Materials and Methods: Mothers of 500 infants and toddlers of ages 3 days to 3 years who were attending GRH, Madurai, were included and provided with a standard questionnaire and results analyzed. Duration of the study was 1 year.

Results: In this study of 500 cases, 40% received antenatal advice. 12.6% mothers breastfed within 1 h while 34.2% breastfed in <6 h. 55.1% of the normally delivered mothers and 4.1% of the cesarean sectioned mothers started breastfeeding within 6 h. 55.2% mothers administered prelacteal feeds to their infants while 44.8% did not. 3/4th expressed their milk when the baby is in NICU. Top feeds started by 63.5% by 4 months, 51% started bottle feeding by 3 months. Early weaning started by 10.54% before 3 months of age mean duration of breastfeeding was 15 months. No correlation was found between the age, parity, nutritional status and family income of the mothers, and breastfeeding practices. A significant correlation was found with the employment status of the mothers.

Conclusion: Majority of mothers had good knowledge of the technique of breastfeeding, and only 4.6% did not show any response. Employment was one of the reasons for the early introduction of bottle feeds. Expression of breast milk is not practiced in this category of mothers due to lack of knowledge regarding the procedure.

Key words: Breastfeeding practices, Employment, Maternal factors, Top up feeds, Weaning

INTRODUCTION

Breastfeeding is a natural and traditional infant feeding practice throughout the world. Pre-modern societies have a high incidence and long duration of breastfeeding. However, in developing countries like India, the newly created economic markets based on highly advanced and imported technologies are promoting the administration of artificial feeds for infants from a very early age.

The prominent area of concern includes minimal feeding of colostrum, delayed initiation of breastfeeding, initiation of prelacteal feeds, nonexclusive breastfeeding in first 6 months of life, early initiation of cows milk, commercial infant feeding, early termination of breastfeeding, and premature introduction of semisolids.

It is a proven scientific fact that all commercial infant milk foods and animal milk are inferior to breast milk, which is nutritious food for infants, readily available, hygienic, and develops emotional bonding and protects against several infections including diarrhea and respiratory infections and saves lives.

Hence, a study of infant feeding practices that is prevalent in any geographical area is essential to outline trends in feeding patterns and before the formulation of any need-based intervention programs.

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MATERIALS AND METHODS

Mothers of 500 infants and toddlers of ages 3 days to 3 years who were attending GRH, Madurai, were included in the study for 1 year. They were provided with a standardized questionnaire based on which data was collected. Maternal characteristics evaluated included age, family income, socioeconomic status, employment status, and mode of delivery. Of 500 mothers, 100 were selected from postnatal ward from 3rd postnatal day onward to get a more accurate account.

RESULTS

In all 500 mothers having children below 3 years were interviewed at Government Rajaji Hospital. 100 mothers were selected from the postnatal ward from the 3rd postnatal day onward to get a more accurate account of the immediate postnatal management of breastfeeding. The infants and toddlers were subdivided into 5 groups for better analysis of various data [Table 1].

The groups were subdivided based on the family income to get better data about their correlation for the duration of breastfeeding and starting top feeds [Figure 1].

The mothers were divided into two groups based on their employment status [Table 2]. In that employed mothers were 18.6% and unemployed was 81.4%. 41% mothers received antenatal counseling regarding benefits and management of breastfeeding, while 59% received no counseling [Figure 2]. The subjects were also divided into two groups based on the mode of delivery, to know accurately about the duration of starting the breastfeeding [Figure 3]. 82.4% had a vaginal delivery, 3% had assisted vaginal delivery, and 14.6% had cesarean section.

It was noticed that timely suckling in the 1st h of birth was practiced only by 12.6% mothers. 34.2% mothers put their infants to breast between 1 and 6 h [Table 3].

It was observed that 55.1% mothers started breastfeeding within 6 h after vaginal delivery, only 4.1% started breastfeeding within 6 h after cesarean section, 72.62% started only after 1 day following cesarean section.

Of 26 mothers, whose baby was in NICU 69.2%, expressed their milk. 55% mothers administered prelacteal feeds to their infants while 45% mothers did not [Figure 4]. Breastfeeding techniques were adapted by 270 mothers with infants below 1 year [Table 4]. Of 187 mothers whose infants were <4 months old, 93% breastfed on demand, while 7% followed scheduled timings.

In this study, it was found that only 30 mothers used pacifiers, 2 on self-decision and one on the advice of paramedical staff. It was noted that of 313 mothers, whose children were more than 4 months old, 8 had stopped breastfeeding before their children attained 4 months of age [Table 5].

In this study, 63.5% mothers have started top feeds in the first 4 months itself even though IAP and WHO recommends exclusive breastfeeds till 6 months of age

Table 1: Age group of child divided into 5 groups

Age group	Number of child (%)
3 days – 1 month	100 (20)
1–4 months	87 (17.4)
5–11 months	83 (16.6)
1–2 years	106 (21.2)
>2 years	124 (24.8)

Table 2: Employment: Employed mothers: 93 (18.6%) unemployed mothers: 407 (81.4%)

Nature of work	Number of cases (%)
Agricultural coolies	51 (54.8)
Manual laborer	15 (16.01)
Company worker	19 (20.4)
Clerk	4 (4.3)
Hospital worker	2 (2.2)
Servant maids	2 (2.2)

Table 3: Time of first breastfeed after delivery

Time	Number of cases (%)
<1 h	63 (12.6)
1–6	171 (34.2)
6–12	89 (17.8)
12–24	74 (14.8)
2 days	72 (14.4)
3 days	24 (4.8)
4 days	2 (0.4)
>4 days	5 (1)

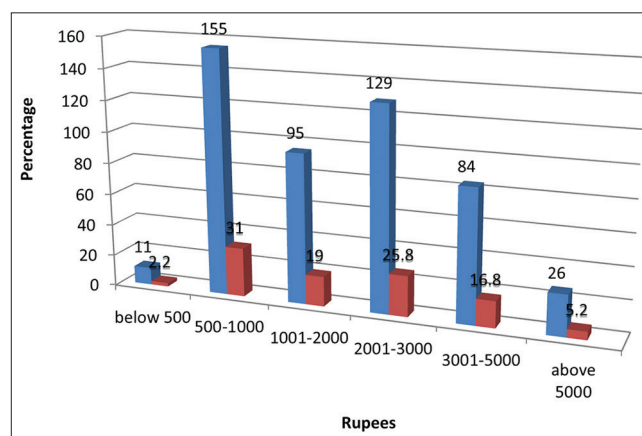


Figure 1: Family income

[Table 6]. It was found that introduction of weaning food was practiced by 10.54% of mothers before 3 months, 91.38% by 5–6 months and all practiced before 1 year [Figure 5].

DISCUSSION

This study conducted in 500 mothers having children aged 3 days to 3 years has revealed that the most common method of infant feeding was breastfeeding. This indicates clearly that the breastfeeding still remains popular and is also in accordance with reports from different parts of India.^[1-5] It was a hospital based study, only 40.2% of mothers had received antenatal counseling [Figure 2]

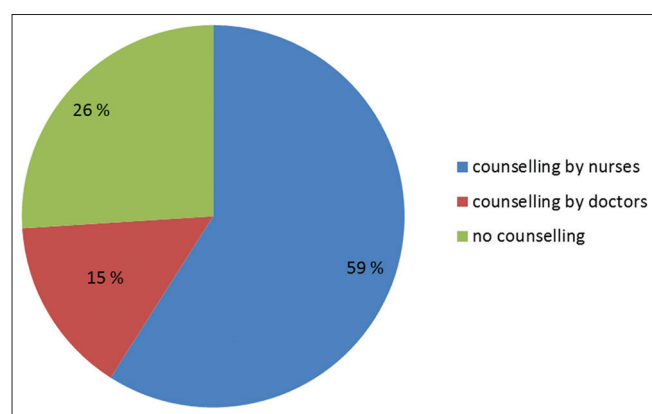


Figure 2: Antenatal counseling

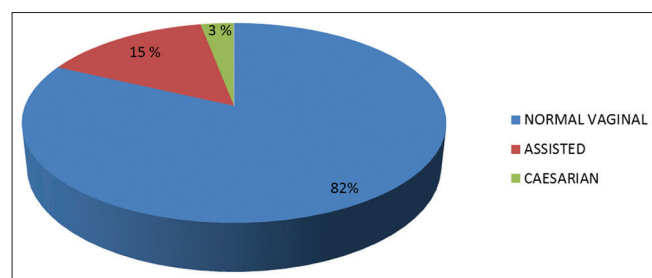


Figure 3: Type of delivery

Table 4: Breastfeeding technique

Technique	n (%)
Position of breastfeeding	
Mostly sitting	263 (97.4)
Mostly lying	7 (26)
Nipple and most of the areola inside the mouth	260 (96.3)
Sucking was painless	232 (85.93)
Complete emptying of one breast only	31 (11.48)
Complete emptying of one breast followed by second	47 (17.4)
Complete emptying of both breasts	192 (71.1)
Knows starting feeding at alternate breasts	207 (76.7)
Know placing the finger between gums and areola to release the suction	146 (54.04)
Burping after feeds	254 (94.07)

regarding breastfeeding; 25.6% from doctors and 14.6% from nursing staff. This may be due to the notion that breastfeeding is the norm, or due to lack of motivation of the medical staff or excessive workload.

The mean duration of breastfeeding in employed class was found to be 9.3 months while in unemployed was 16.3 months. A significant correlation was found between the duration of breastfeeding and employment status of the mothers. This was partly due to the unfavorable working condition. As in other studies, there was no correlation of duration of breastfeeding with age, parity, religion, nutritional status, family income, and maternal education.

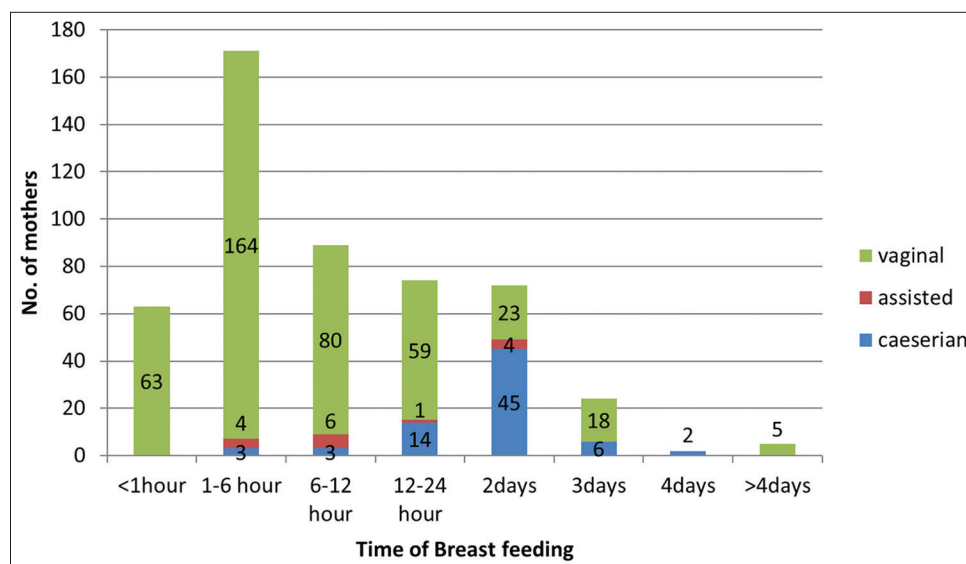
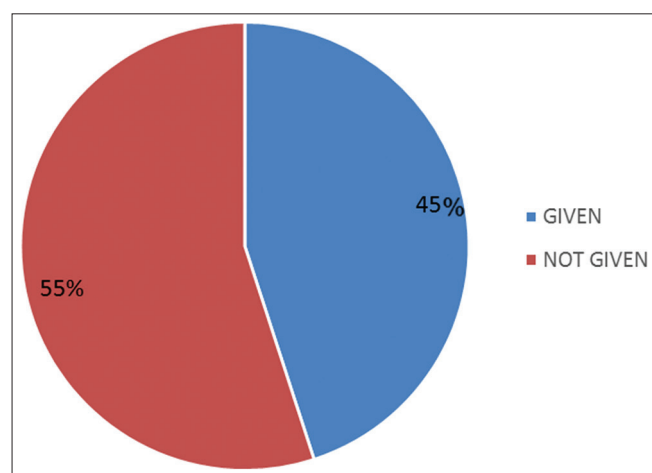
In this study suckling in the 1st h of birth was only 12.6% and even within 6 h was only 46.8% [Table 3], by applying Chi-square test, we tried to deduce the association between the time of first breastfeed after delivery with the type of delivery and found to be very highly significant. 55.1% of normally delivered mothers started breastfeeding within 6 h but only 4.1% after cesarean section [Figure 4]. Expressed milk was given by 18 (69.2%) of 26 mothers, whose baby were in NICU. Advice regarding the expression of breast milk was given by medical staff in 7 cases.

Prelacteal feeds were given to 55.21% of infants [Figure 5]. Kumar *et al.* and Srivastava *et al.* have also reported a similar percentage of giving prelacteal feeds in their studies. The prelacteal feeds received are plain water, glucose water, honey, fruit juice, tea, milk powder, and oil with Jaggery. Prelacteal feeds were given by spoon, filler, cloth wick, bottle, finger, and with golden ring. These unhygienic modes of administration of giving prelacteal feeds were more commonly observed in lower income and less educated mothers. The practice of giving prelacteal feeds is common in many parts of the country, the preparations varying from place to place. They are the source of infection; there is a high probability of these prelacteal feeds getting aspirated. The fact that the small amount of milk produced during the 1st few days is sufficient for the newborn was not well appreciated by the mothers. In the present study, colostrum was not denied to any baby due to any wrong notion of it being bad. However, in studies of Kumar *et al.* and Srivastava *et al.*^[2,3] colostrum were given only to 16% and 17%, respectively.

Of 187 mothers with their infants below 4 months, 8 mothers gave scheduled feeds, and 179 mothers were giving breastfeeds on demand. Of 187 mothers with their infants aged below 4 months, 30 mothers used pacifiers. Use of pacifiers has to be strongly discouraged as it will result in poor sucking technique, the risk of infection and missed opportunity to breastfeed.

Table 5: Duration of breastfeeding

Age group month	Total no	Mother continuing bf	Mothers who stopped breastfeeding at months									
			1	2	3	4	5-6	6-10	11	12-15	16-24	>24
0-1	100	100										
1-4	87	83	4									
5-11	83	63	2			2	4	12				
1-2 years	106	22				4	8	12		40	20	
2-3 years	124						12	4	10	40	40	18


Figure 4: Correlation of time of first breast feed with mode of delivery

Figure 5: Prelacteal feeds

In this study, it was found that 97.4% of mothers were breastfeeding at 4 months, 78.3% at 1 year, and 14.5% at 2 years. Similar trends were noticed in other studies. The reason for stopping breastfeeding is mentioned in Table 6.

Regarding mother's knowledge of the advantages of breastfeeding it was observed that 79.3% of mothers knew that mothers milk is the best milk,^[6,7] 55% knew

that baby remains healthy, 40.4% suggested that it is pure and cost nothing, 35.1% knew that it is more nutritious and hygienic, and 25.9% knew that there is less chance of infection [Table 7].

Regarding starting top feeds, 63.5% started top feeds in the first 4 months of life, and 8% by 6 months of life [Table 8] [8-10] WHO recommended exclusive breastfeeding in the first 6 months of life. Exclusive breastfeeding means that except for breast milk no other food or fluids, including prelacteal feeds and water should be given.

In this study, it was found that 10.54% of mothers started weaning with semisolids by 3 months and 51.4% by 4 months [Figure 6]. The early introduction may become a substitute instead of a supplement. Early weaning also affects impoverished families in terms of cost of food and possibly illness needing medical attention.

Due to the popularity gained by tinned infant weaning foods, it was noted that this accounted for 44.07% of the first weaning food. This trend was prevalent even in the low-income group. They cost 10 times higher than the natural food and hence its use has to be discouraged. Other

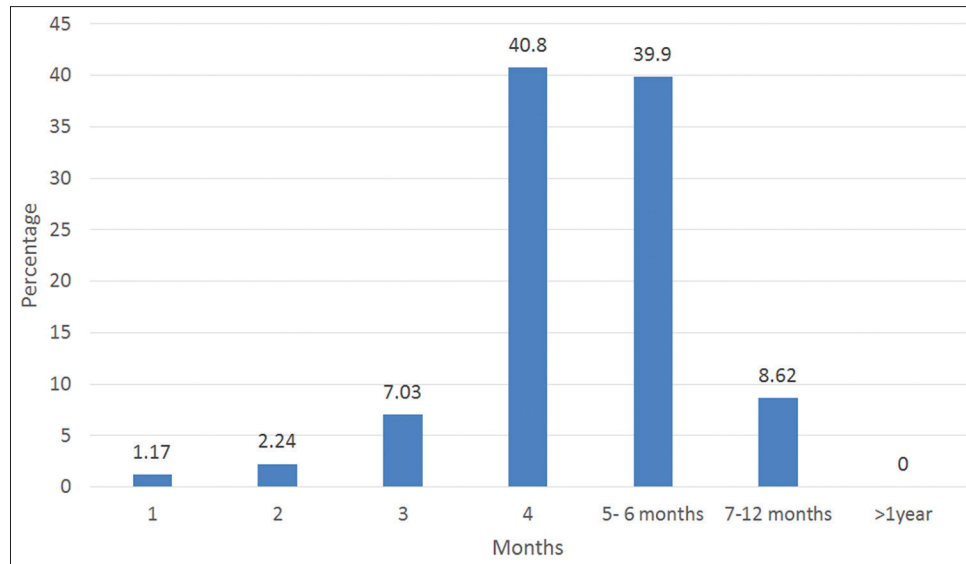


Figure 6: Introduction of weaning foods

Table 6: Reasons for stopping breastfeeding

Reasons	n (%)
Felt that breast milk was inadequate	156 (67.2)
Infant was taking top feeds and breast milk decreased	47 (20.2)
Infants refused to breastfeed	
Decreased breast milk	38 (16.3)
Introduction of bottle	32 (13.7)
Introduction of other milk	
Introduction of cereals	25 (10.8)
Introduction of sweeter weaning foods	36 (15.5)
Addition of sugar or sugar candy	
Mothers ill health	7 (3.01)
Subsequent pregnancy	39 (16.8)
Working mother	33 (14.2)
Figure conscious	0
Embarrassment in breastfeeding	0
Local breast problems	0
Cracked nipple	
Inverted nipple	
Felt that duration of breastfeeding was adequate	41 (17.7)
Infant refused to take other feeds	27 (11.6)

Table 7: Maternal concept of advantages of breastfeeding

Advantages	n (%)
It is pure and costs nothing	193 (40.4)
Clean and sterile	124 (25.9)
No pots and pan	71 (14.9)
Child remains healthy	263 (55.0)
Skin to skin contact	83 (17.4)
Less infection	124 (25.9)
More nutritious and hygienic	168 (35.1)
Gives natural immunity	105 (22)
Helps in preventing further conception	43 (9)
Mothers milk is the best milk	379 (79.3)
No response	22 (4.6)

Table 8: Introduction of top milk in first 4 months

Age in months	Tinned milk (%)	Cow's milk (%)
1 month	0	44 (11)
2 months	17 (4.25)	42 (10.5)
3 months	36 (9)	27 (6.75)
4 months	22 (5.5)	66 (16.5)

weaning foods included rice, mashed banana, potato, and biscuits as the first weaning food.

CONCLUSION

In this study of 500 cases, 40% received antenatal advice from medical personal. Initiation of breastfeeding within 6 h after delivery was found in about half the study participants and it was very poor after cesarean section. 3/4th expressed their milk when the baby is in NICU. Mean duration of breastfeeding was 15 months in the unemployed group. It was much less in employed class. The practice of prelacteal feeds is still continuing, and in a large number of cases, advice was given by medical and paramedical personnel. Colostrum feeding is uniformly practiced irrespective of socioeconomic and literacy levels. Majority of mothers had good knowledge of the technique of breastfeeding, and only 4.6% did not show any response. Top feeds started by 63.5% by 4 months and 51% started bottle feeding by 3 months. Early weaning was practiced by 10.54% before 3 months of age. Employment was one of the reasons for the early introduction of bottle feeds. Expression of milk was not practiced in this category of mothers due to lack of knowledge regarding the procedure.

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Comparison of Management Strategies in Chronic Subdural Hematoma: A Retrospective Study

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Abstract

Introduction: Chronic subdural hematoma is one of the most common diseases encountered in neurosurgical practice. Although surgical drainage is an established treatment option for symptomatic patients, the ideal surgical approach remains controversial. The superiority of one modality over the other remains to be established.

Aim: This study aims to compare burr hole tapping and craniotomy in the management of chronic subdural hematoma.

Materials and Methods: A retrospective analysis of 100 cases of chronic subdural hematoma admitted in our institution was done. The type of procedure, operative duration, post-operative stay, reoperation, post-operative Glasgow coma scale, and mortality were analyzed using Chi-square test.

Results: The ideal procedure for each patient is shown based on the analysis of various parameters and their statistical significance is interpreted.

Conclusion: The ideal surgical option for chronic subdural hematoma has been highlighted based on the studied parameters. The best possible benefit to the patient has been elucidated.

Key words: Burr hole, Chronic subdural hematoma, Craniotomy

INTRODUCTION

Chronic subdural hematoma is one of the most common diseases encountered in neurosurgical practice. The condition can be easily diagnosed on plain computed tomography (CT) scans. The reported incidence is approximately 3/100,000 and rises appreciably in the elderly population.^[1]

Chronic sub-dural hematoma was first reported by Wepfer in 1657. It was initially thought of as a form of stroke in the 17th century. Later it was considered as an inflammatory disease in the 19th century and as traumatic in the early 20th century. We now know that trauma is not the mandatory precursor of this condition.

Although surgical drainage is an established treatment option for symptomatic patients, the ideal surgical approach remains controversial.^[2] The procedures adopted in the surgical management for the treatment of chronic subdural hematomas (CSDHs) include twist drill craniostomy, single or multiple burr hole drainage, burr hole trephination, and craniotomy.^[3]

Recent articles state that burr hole drainage is a superior technique compared to twist drill craniostomy and craniotomy due to a lower incidence of recurrence and morbidity.^[3-6] However, no Class I data comparing these treatments^[3] have been established to eliminate the debate over the optimal surgical approach.

The clinical outcome of a particular surgical procedure depends on various other factors which have to be addressed to determine the ideal approach.

At our institution, the surgical drainage procedures presently being performed to treat CSDH are burr hole washout, decompressive craniotomy, burr hole trephination, and

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“mini”-craniotomy. Proponents for performing a craniotomy argue that the wide exposure allows for loculations to be broken up and membranes to be opened, which, in turn, leads to increased amount of subdural drainage and decrease in recurrence rates.^[7,8] The aim of this study was to compare burr hole drainage and craniotomy in the management of chronic subdural hematoma and to determine their clinical benefits.

Aim of the Study

The aim of the study was as follows:

1. To compare the burr hole drainage and craniotomy in management of chronic subdural Hematoma
2. To establish the optimum procedure for the given patient
3. To establish statistical significance in selection of procedure
4. To aid in prognostication of surgery for chronic subdural hematoma.

MATERIALS AND METHODS

Study Group

This study was conducted at the Department of Neurosurgery, Madurai Medical College, Madurai, from January 1, 2016, to June 31, 2017. 100 patients who underwent surgical drainage of a chronic subdural hematoma were retrospectively selected. Of 100 patients, 60 patients underwent burr hole tapping and 40 patients underwent various types of craniotomy which includes mini-craniotomy, decompressive craniotomy, and burr hole trephination.

Table 1: Age-wise distribution

Age in years	Group		Total
	Burr hole	Craniotomy	
<45	11	2	13
>60	27	17	44
45–60	22	21	43
Total	60	40	100

Table 2: Chi-square tests for age

	Value	df.	Asymptotic significance (two-sided)
Pearson Chi-square	4.715 ^a	2	0.095
Likelihood ratio	5.148	2	0.076
Number of valid cases	100		

Table 3: Sex distribution

Sex	Burr hole	Craniotomy	Total
Female	7	5	12
Male	53	35	88
Total	60	40	100

Method Used

The initial CT scan performed on arrival and the 24 h post-operative CT scan were studied.

The volume of subdural hematoma in the initial CT was measured using the formula $A \times B \times C / 2$, where A, B, and C represent the dimensions in three axes perpendicular to each other.^[9] The change in the clot volume on the pre- and post-operative CT scans was calculated and recorded. The difference was then computed and the percentage of the clot removed was determined.

Medical records were reviewed for patient demographics.

The following parameters were also noted from patient records:

1. Glasgow coma scale (GCS) preoperatively on the 1st post-operative day and at discharge were noted.
2. Admission and discharge Rankin disability score
3. Pre-operative comorbidities
4. Use of anticoagulation/antiplatelet therapy
5. History of alcohol abuse
6. Time in the operating room.

Various factors that are considered to be risk factor of CSDHs such as head trauma, underlying disease having bleeding tendency, and medications that alter coagulation status were corrected before surgery.

Table 4: GCS score distribution

	Burr hole group	Craniotomy	Total
GCS			
<7	3 (5.0)	1 (2.5)	4 (4.0)
8–12	29 (48.3)	10 (25.0)	39 (39.0)
>13	28 (46.7)	29 (72.5)	57 (57.0)
Total			
Count	60	40	100

GCS: Glasgow coma scale

Table 5: GCS score cross tabulation

	Value	Df.	Asymptotic significance (two-sided)
Pearson Chi-square	6.535 ^a	2	0.038
Likelihood ratio	6.699	2	0.035
Linear-by-linear association	5.796	1	0.016
Number of valid cases	100		

GCS: Glasgow coma scale

Table 6: Reoperation group cross tabulation

Reoperation	Burr hole group	Craniotomy	Total
No	50	38	88
Yes	10	2	12
Total	60	40	100

Table 7: Chi-square tests for reoperation

Parameter	Value	Df.	Asymptotic significance (two-sided)	Exact significant (two-sided)	Exact significant (one-sided)
Pearson Chi-square	0.050 ^a	1	0.824		
Continuity correction ^b	0.000	1	1.000		
Likelihood ratio	0.050	1	0.823		
Fisher's exact test				1.000	0.527
Number of valid cases	100				

Reoperation was done, 10 cases in burr hole group and 2 cases in craniotomy

Table 8: Reoperation in age wise

Reoperation rate	Burr hole group	Craniotomy
<40 years	Nil	Nil
41–60	2	1
>61	8	1

Table 9: Operative time - cross tabulation

Time (min)	Burr hole group	Craniotomy	Total
<50	56	6	62
50–100	4	25	29
>100	0	9	9
Total	60	40	100

Table 10: Operative time - Chi-square tests

Chi-square tests	Value	df.	Asymptotic significance (two-sided)
Pearson Chi-square	63.052 ^a	2	0.000
Likelihood ratio	71.909	2	0.000
Linear-by-linear association	56.298	1	0.000
Number of valid cases	100		

Table 11: Post-operative stay - cross tabulation

	Burr hole group	Craniotomy	Total
≤10 days	54	26	80
>10 days	6	14	20
Total	60	40	100

The choice of operation was based solely on the surgeon's preference and clinical experience.

Statistical Methods

The following statistical methods were used.

The data were analyzed using the Chi-square test.

OBSERVATIONS AND RESULTS

Patients undergoing burr hole tapping will be grouped as Group 1 and craniotomy as Group 2 hereinafter.

In the age group of <45 years, 11 patients in burr hole group and two patients in craniotomy group [Table 1].

In the age group between 45 and 60 years, 22 patients in burr hole group and 21 patients in craniotomy group.

In the age group of >60 years, 27 patients in burr hole group and 17 patients in craniotomy group.

P value of age group is 0.095 which is statistically not significant [Table 2].

The mean age in burr hole group is 57.5 years of age and mean age in craniotomy group is 59.45 years.

Of 60 patients in burr hole group, 53 are male patients and seven are female patients [Table 3]. Of 40 patients in craniotomy group, 35 patients are male patients and five patients are female patients.

Three patients in burr hole group and one patient in [Table 4 and 5] craniotomy group presented in GCS <7, 29 patients in burr hole group and 10 patients in craniotomy group presented in GCS 8–12, and 28 patients in burr hole group and 29 patients in craniotomy group presented in GCS >13.

Reoperation was less in craniotomy group when compare to burr hole group, but *P* = 0.824 which is statistically not significant.

Reoperation is needed more in the age group of above 60 years, especially in the burr hole tapping group [Table 6 and 8].

Operative time is less for burr hole tapping group, most of the cases are finished before 50 min, *P* value for operative is <0.001 which is statistically highly significant.

Post-operative stay is <10 days seen in 54 patients in burr hole tapping and 26 patients in craniotomy groups. *P* = 0.002 which is statistically significant

Table 12: Chi-square tests post-operative stay

	Value	df.	Asymptotic significance (two-sided)	Exact significant (two-sided)	Exact significant (one-sided)
Pearson Chi-square	9.375 ^a	1	0.002		
Continuity correction ^b	7.878	1	0.005		
Likelihood ratio	9.275	1	0.002		
Fisher's exact test				0.004	0.003
Linear-by-linear association	9.281	1	0.002		
Number of valid cases	100				

Table 13: Death in each group cross tabulation

Outcome	Burr hole group	Craniotomy	Total
Death	10	14	24
Discharged	50	26	76
Total	60	40	100

Table 14: Chi-square tests for death

	Value	df.	Asymptotic significance (two-sided)	Exact significance (two-sided)	Exact significance (one-sided)
Pearson Chi-square	4.423 ^a	1	0.035		
Continuity correction ^b	3.475	1	0.062		
Likelihood ratio	4.353	1	0.037		
Fisher's exact test				0.055	0.032
Number of valid cases	100				

Table 15: Procedure wise - cross tabulation

Procedure	Death	Discharged	Total
Burr hole tapping	10	50	60
Burr hole trephination	2	1	3
Craniotomy	7	13	20
Decompressive craniectomy	3	2	5
Mini-craniotomy	2	10	12
Total	24	76	100

Table 16: Death in age wise

Age	Burr hole	Craniotomy
40	1	4
40–60	3	4
>60	6	6

Table 17: Comorbidities

Comorbidities	Burr hole group	Craniotomy group
Bleeding diathesis	18	10
Heart disease	28	8
DM	5	3
HT	32	18
Others	5	3

Ten patients were dead in burr hole group and 14 patients were dead in craniotomy group. *P* value for death cross tabulation is 0.035 which is statistically not significant.

DISCUSSION

Chronic subdural hematoma is a common disease encountered in neurosurgical practice. The various surgical procedures such as twist drill craniostomy, burr hole drainage, and craniotomy result in varying degrees of reoperation rates from 5% to 27.8%^[10-13] as well as varying morbidity and mortality rates. However, due to the discrepancy in clinical outcome of each surgical intervention, there is an ongoing debate over optimal surgical treatment [Table 7].

Hamilton *et al.*^[14] concluded that there was no significant difference in the incidence of post-operative complications, hematoma recurrence, or operative mortality among the different surgical groups. Mondorf *et al.*^[15] described a comparison between craniotomy and burr hole treatments where the number of craniotomy patients more than tripled that of the burr hole group.^[15] He reported craniotomy remains a valid and safe technique for the management of patients with chronic subdural hematoma. [Table 9 and 10]

Sambasivan compares 2300 cases of CSDH where over 2200 are treated with craniotomy and only 51 with burr hole drainage [Table 11 and 12].^[13] They concluded that an extended surgical approach with partial membranectomy has no advantages regarding the rate of reoperation and

the outcome. However, Lee *et al.* compared 38 patients with burr hole drainage to 13 treated with craniotomy^[11] [Tables 13-16] and inferred that as initial treatment, burr hole drainage with irrigation of the hematoma cavity and closed-system drainage is recommended. Extended craniotomy with membranectomy is reserved for instances of acute rebleeding with solid hematoma.

The surgical technique for “mini-craniotomy” involved raising a craniotomy flap of about 5–7 cm in greatest diameter centered over the area of maximal hematoma thickness. The outer membrane was opened and excised as far as the craniotomy edges and then the inner membrane would be excised.

In cases of burr hole and tapping, the burr hole was placed in the frontal region at the Kocher’s point and the other placed at the parietal eminence. The outer membrane was opened and irrigation was performed until clear effluent.

The primary endpoints of the study included reoperation rates and mortality. Secondary endpoints involved length of post-operative stay and morbidity as measured by post-operative and discharge Glasgow coma score, and discharge disposition. The data collection concluded when the patient was either discharged or expired. There was no long-term follow-up.

In addition, there were a higher number of post-operative complications for craniotomy in our data, specifically related to post-operative infections, acute hemorrhage, and metabolic disturbances. Mortality associated with both procedures was comparable. With similar morbidity and mortality rates, our data support burr hole washout over craniotomy for the treatment of CSDH in elder patients. In case of reoperation, mini-craniotomy was superior to burr hole tapping and decompressive craniotomy.

The secondary endpoints of the study, the average length of stay, and average time in the operating room were compared. The results show that burr hole tapping as a better procedure compared to craniotomy as there was shorter duration of hospitalization (7.7 vs. 11.1 days) and less time spent in the operating room. (48.8 vs. 129.4 min).

The major limitations of our study remain that this is a retrospective study and includes relatively small number of patients when compared to other studies. Due to the retrospective nature, there is a lack of long-term follow-up in our study. As it may be difficult to generalize the conclusions from the smaller sample size, the difference in

patient safety requires further investigation. Future long-term multi-institutional, prospective studies are needed to fully demarcate the differential outcomes due to procedure choice [Table 17].

CONCLUSION

In the age group of <60 years, burr hole tapping appears to be superior to craniotomy for the treatment of CSDH with respect to patient outcome, operating time, length of stay, and recurrence. In our study, older age group had more recurrence rates with burr hole tapping when compare to craniotomy. In that case of reoperation, mini-craniotomy was superior to burr hole tapping and decompressive craniotomy. However, in case of severe comorbid conditions such as heart disease, renal diseases, and lung disorders, initial burr hole tapping may be appropriate.

Mini-craniotomy appears superior to other procedures in elder patients, whereas burr hole tapping is optimal method in younger adult subjects, but future long-term prospective, multicenter studies are needed.

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Role of Imaging Modalities in the Management of Urinary Tract Infection in Children

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Abstract

Background: Urinary tract infections (UTIs) are a common clinical condition in pediatric practice requiring special attention as congenital anomalies of kidneys and collecting system is usually the causes of recurrence. American Academy of Pediatrics recommends children with UTI should be investigated with voiding cystourethrogram (VCUG), ultrasonogram of urinary tract (renal ultrasound [RUS]), and radionuclide imaging of kidney (dimercaptosuccinic acid renal scan) for diagnosing underlying urinary tract abnormalities.

Aim of the study: The aim of the study was to assess the role of routine RUS in the management of young children hospitalized with uncomplicated febrile UTI.

Materials and Methods: A total of 120 children between 1 month and 12 years of age with the first episode of a confirmed diagnosis of UTI were included in this prospective cross-sectional study. All the children were thoroughly investigated after elicitation of history. Culture of urine, ultrasonogram (RUS) and radionuclide renal scan were obtained at the time of admission. VCUG was performed after 6 weeks to look for vesicoureteric reflux. These tests are in addition to routine investigations before and during follow-up of treatment.

Observations and Results: RUS was done in 120 cases, and 14 (11.66%) cases had abnormal findings. Hydronephrosis is seen in 8 cases (7%), cystitis in 4 cases (3%), pelvic-ureteric junction obstruction in 2 cases (1.8%). VCUG was done in 40 cases (31 males and 9 females) and was abnormal in 12 (30%) cases. 4 (10%) and 2 (5%) of 40 cases had Grades 1–2 vesicoureteral reflux (VUR) and Grades 3–4 VUR, respectively. 4 (13%) of 31 males and 2 (22%) of 9 females who underwent VCUG had evidence of VUR; this female to male ratio of 1.7:1 found was not significant statistically ($P = 0.49$). The sensitivity, specificity, positive predictive value, and negative predictive value of RUS for detecting VUR were 20.7%, 87.33%, 26.33%, and 83.33%, respectively [Table 1]. For the purpose of further analysis, the children were divided into three age groups: <1 year (28 children and 20/08 male/female), 1–5 years (60 children and 44/16 male/female), and 5–12 years (32 children and 12/20 male/female).

Conclusions: The present study question the yield of routine RUS in the management of young children with simple UTI. The study concludes that RUS should only be performed in children in whom complications such as renal obstruction or abscess are suspected based on an unfavorable clinical course, or in children in whom VUR has been found, to look for renal structure abnormalities.

Key words: Bacteriuria and children, Renal ultrasound, Urinary tract infection, Voiding cystourethrography

INTRODUCTION

The main goals of imaging studies in children with episodes of urinary tract infection (UTI) are to identify urinary tract

anatomic abnormalities. Unless the existences of such abnormalities are investigated, therapeutic measures even though executed would not prevent future infections and possible long-term damage to the kidneys. Renal ultrasound (RUS) remains currently the most recommended imaging study which mainly detects abnormalities in the upper urinary tract such as hydronephrosis or pelvic-ureteric obstruction. This is followed by voiding cystourethrography (VCUG) or radionuclide cryptography (RNC) to detect anomalies of the lower urinary tract, mainly vesicoureteral reflux (VUR).^[1,2] RUS remains an ideal tool of investigation in the hands of the pediatrician

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due to its non-invasive nature, the lack of radiation, and the low cost of the procedure for the children with UTI.^[3,4] RUS, when performed during the hospitalization may also detect pathologies such as obstructive uropathy or an abscess that directly influences the management of the child. Review of literature shows that the RUS data have low sensitivity and specificity for predicting VUR. Also especially, when the mothers have undergone repeated ultrasound examination during their pregnancy, the major anomalies would have been diagnosed in the children with UTI. These data question the importance of routine RUS in the management children with acute uncomplicated UTI.^[5-8] In this study an attempt is made to assess the role of routine RUS in the management of young children hospitalized with uncomplicated febrile UTI.

MATERIALS AND METHODS

Study Design

This was a cross-sectional prospective and analytical study.

Institute of Study

This study was conducted at the Department of Paediatrics, IMCH, Government Medical College, Kozhikode.

Period of Study

This study was from March 2014 to August 2015.

The present study was a prospective, cross-sectional and analytical study conducted in the Department of Pediatrics of a tertiary teaching hospital of Kerala. An ethical committee clearance was obtained to conduct the study. 120 children on the study group were chosen according to the following criteria:

Inclusion criteria

1. Children between 1 month and 12 years of age, who presented with uncomplicated febrile UTI were included.
2. Children with UTI; presenting with a combination of a positive urine culture (growth of >100 bacteria/ml in a midstream sample or any growth in suprapubic bladder aspiration or in/out bladder catheterization) and fever >38.0°C were included.

Exclusion criteria

1. Children with uncomplicated UTI determined as a child with febrile UTI who clinically responded and became afebrile within 48 h of initiation of therapy were excluded.
2. Children with known urinary tract anomalies, and/or who had been treated with antibacterial agents within 7 days before the admission were excluded.
3. Children below 1 year and above 12 years were excluded.

The sample of the study was calculated based on the prevalence rate VUR in 20% of young children with first diagnosed UTI. A study sample of 200 children was included in the study satisfying the criteria of inclusion and exclusion. The urine was obtained for culture and sensitivity by suprapubic aspiration or in and out bladder catheterization in children younger than 2 years and by the midstream techniques in older children. All the children were initially treated with intravenous antibacterial agents (ampicillin + gentamicin or cefuroxime). Intravenous therapy was continued until fever had subsided, but for at least 96 h in neonates or 48 h in older infants and children. Later followed by oral therapy with appropriate agents was continued for a total duration of 10–14 days. Preventive therapy was given thereafter until results of the VCUG were available. RUS was performed in all patients during the hospitalization using an ultrasound machine with sector or linear 7 and 7.5 MHz transducers. It consisted of an examination of the kidneys to show the kidney size, renal outlet obstruction (such as pelvic-ureteric junction stenosis), collecting system dilatation, parenchymal structure, and parenchymal lesions such as an abscess. Furthermore, examination of the bladder was done to identify dilatation of the distal ureters, hypertrophy of the bladder wall, and presence of ureteroceles. Renal pelvis dilatation was defined as suggestive of VUR and graded as mild, moderate, or severe (hydronephrosis).^[9] A VCUG was performed within 2–6 months after the infection, and VUR was classified according to the international VUR classification.^[10] The impact on management was defined as a change of therapy, investigations, or follow-up based on RUS results, that would not have been done otherwise. All the data collected were analyzed using standard statistical methods.

OBSERVATIONS AND RESULTS

Age and Gender Distribution

Of 120 cases studied, 28 (23.3%) cases were below 1 year, 60 (50%) cases were between 1 and 5 years, and 32 (26.6%) cases were between 5 and 12 years [Figure 1].

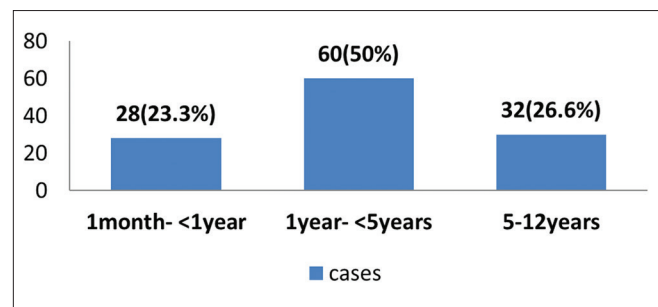


Figure 1: Age incidence in the study group (n=120)

Gender Distribution

In the study population, 76 (63.4%) were males and 44 (36.6%) were females. Males outnumber females in children <5 years (71.4% in children between 1 and 12 months and 73.3% in children between 12 and 59 months). Females (62.5%) outnumber males >5 years [Figure 2].

Spectrum of Isolated Organisms

88 (73.3%) *Escherichia coli*, 21 (17.5%) *Klebsiella*, 3 each of *CONS*, *Enterobacter*, *Staphylococcal aureus*, and 2 of *Acinetobacter* species were isolated. Most common organism isolated was *E. coli* followed by *Klebsiella* [Figure 3].

RUS

RUS was done in 120 cases, and 14 (11.66%) cases had abnormal findings. Hydronephrosis is seen in 8 cases (7%), cystitis in 4 cases (3%), and pelvic-ureteric junction obstruction in 2 cases (1.8%) [Figure 4].

All the hydronephrosis (8 cases) was detected in children <5 years. Of 8 cases with hydronephrosis

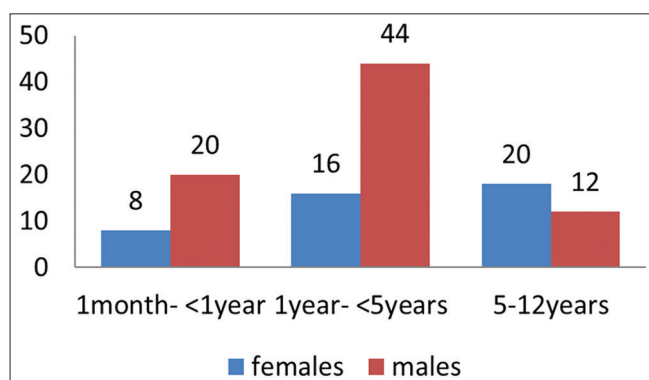


Figure 2: Gender incidence in the study (n=120)

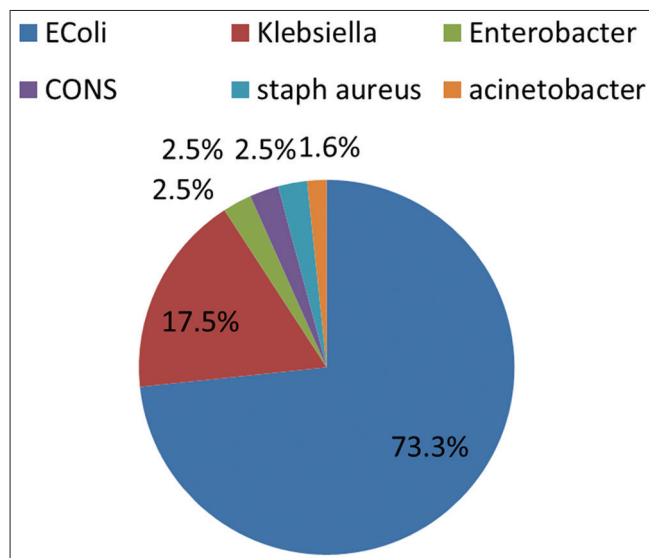


Figure 3: Distribution of organism cultured in the study (n=120)

7 (87.5%) were males and 5 (71.4%) of these 7 males with hydronephrosis had posterior urethral valve (PUV) [Figure 5].

VCUG

VCUG was done in 40 cases (31 males and 9 females) and was abnormal in 12 (30%) cases. 4 (10%) and 2 (5%) of 40 cases had Grades 1-2 VUR and Grades 3-4 VUR, respectively. 4 (13%) of 31 males and 2 (22%) of 9 females who underwent VCUG had evidence of VUR; this female to male ratio of 1.7:1 found was not significant statistically ($P = 0.49$). In 31 males who underwent VCUG 6 (19.35%) had PUV. Of 6 PUV cases, 4 cases (66.7%) were detected before 12 months of age; 2 (33.3%) cases of PUV were detected after the age of 12 months [Figure 6].

Dimercaptosuccinic Acid (DMSA) Renal Scan

DMSA was done in 57 cases and detected abnormality in 21 cases (37%). All children with abnormal DMSA renal scan (21 cases) had renal scarring at 2-3 months after 1st episode UTI. None of the children had renal function impairment which was assessed by split renal function on DMSA renal scan [Figure 7].

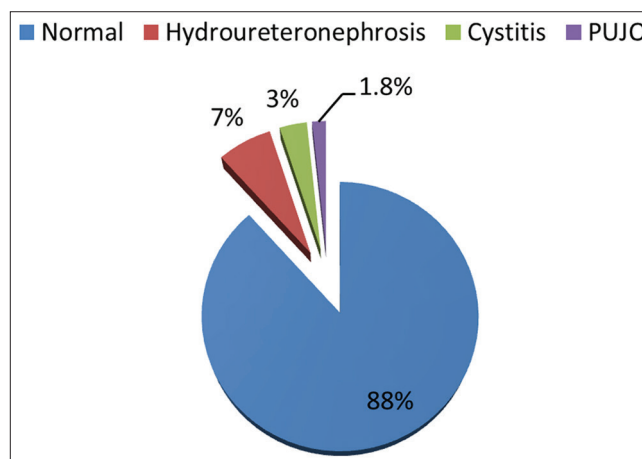


Figure 4: Incidence of abnormal ultrasonography findings (n=120)

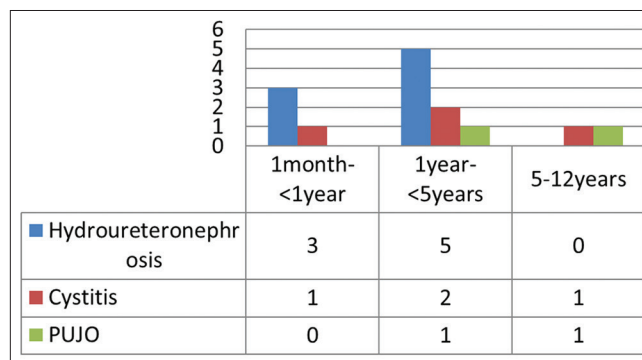


Figure 5: Age incidence of the abnormalities diagnosed on ultrasonography (n=14)

Treatment Outcome

Of 120 cases, 48 (40%) cases responded (became non-toxic and devoid of urinary symptoms) within 5–7 days of antibiotics. 47 cases needed antibiotics for 7–10 days and 25 cases needed antibiotics for 10–14 days for complete clinical recovery [Figure 8].

Surgical interventions: 6 (7.9%) of 76 males studied had PUV. All children with PUV had undergone cystoscopic fulguration, and 4 of these 6 children had undergone pyeloplasty after fulguration [Figure 9].

The sensitivity, specificity, positive predictive value (PPV), and negative predictive value of RUS for detecting VUR were 20.7%, 87.33%, 26.33%, and 83.33%, respectively [Table 1]. For the purpose of further analysis, the children were divided into three age groups: <1 year (28 children and 20/08 male/female), 1–5 years (60 children and 44/16 male/female), and 5–12 years (32 children and 12/20 male/female). The sensitivity, specificity, PPV, and negative predictive value of abnormal RUS for detecting VUR were 29%, 81%, 21%, and 87%, respectively, in the <1 year group, 25%, 87%, 26%, and 88%, respectively, in the 5 years group, and 9%, 94%, 32%, and 75%, respectively, in the 5–12 years group. The differences in sensitivity and specificity between these groups had no statistical significance [Table 1].

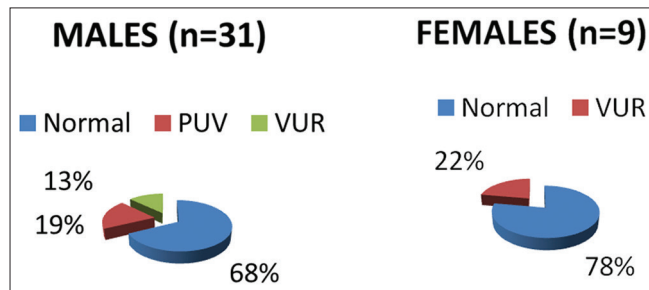


Figure 6: Incidence of micturating cystourethrogram findings (n=12)

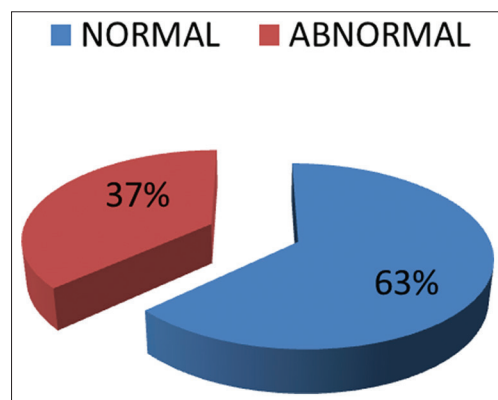


Figure 7: Incidence of abnormal dimercaptosuccinic acid results (n=120).

DISCUSSION

UTI is one of the most frequently encountered clinical entities in pediatrics practice. It has been estimated that 8% of girls and 2% of boys will have a UTI during childhood.^[11] UTI serves as a marker of underlying anatomic and functional abnormalities. Infants and young children are at higher risk than older children for incurring acute renal injury. The present study it was observed that RUS findings in children younger than 5 years admitted to hospital with an uncomplicated febrile UTI are of little diagnostic value and have no influence on their management. Review of literature also shows similar results regarding the usefulness of RUS as a screening tool for VUR in children younger than 5 years. Mahant *et al.*^[12] in their retrospective study of 162 children aged below 5 years with UTI, who had undergone investigations RUS and VCUG: RUS was suggestive of VUR if dilatation of the pelvi-calyces, dilatation of the ureters, or dilatation of the collecting system of one or both kidneys were reported. The overall prevalence of VUR was 22%. RUS findings were suggestive of VUR in only 14 of 35 children with confirmed VUR, and in 30 of 127 children without

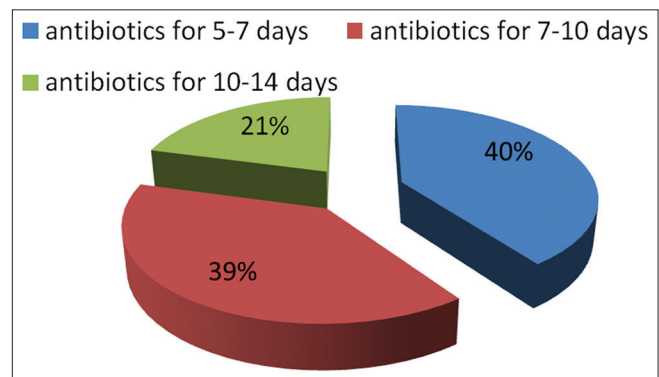


Figure 8: Treatment outcome in the study (n=120)

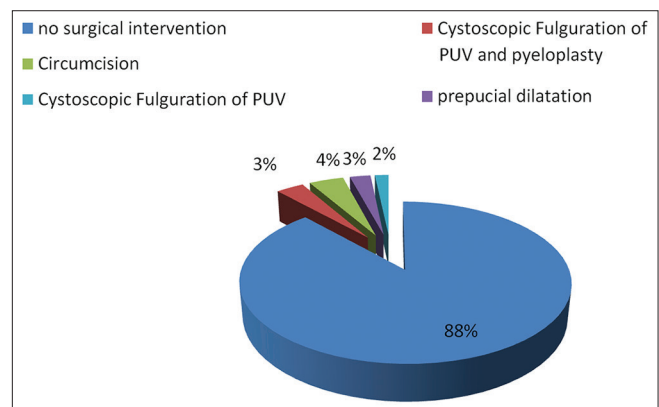


Figure 9: Types of surgical interventions undertaken in the study (n=120)

Table 1: Sensitivity, specificity, PPV, and negative predictive value of RUS for detecting VUR by VCUG (n=120)

Age group (years)	n- M/F	RUS suggestive of VUR	VUR on MCU	VUR in patients with abnormal RUS	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
<1	28-20/8	4	4	3	29	81	21	87
2-5	60-44/16	8	6	2	25	87	26	88
5-12	32-12/20	2	2	3	9	94	32	75
Overall	120	14	12	8	20.7	87.33	26.33	83.33

RUS: Renal ultrasound, VUR: Vesicoureteral reflux, MCU: Micturating cystourethrogram, VCUG: Voiding cystourethrogram, PPV: Positive predictive value, NPV: Negative predictive value

VUR. The sensitivity, specificity, and positive and negative predictive values of ultrasound for VUR were 40%, 76%, 32%, and 82%, respectively. Kass *et al.*^[13] evaluated 453 children with RUS, VCUG, and DMSA renal scan. They showed that of 101 children who had a normal RUS and normal DMSA, 23% had VUR using VCUG. Alon and Ganapathy^[7] studied 124 patients with UTI, of whom RUS showed hydronephrosis and/or hydroureter in 10 patients (8.1%); however, by VCUG, 38 patients (38%) were found to have VUR. Di Pietro *et al.*^[14] reported 70 children under the age of 5 years, who were studied using both RUS and VCUG. Five children (7%) had abnormal RUS, of whom two had VUR on VCUG. Of the other 65 children with normal RUS, 19 (29%) had VUR on VCUG. Smellie *et al.*^[15] evaluated four methods of investigation in 58 children following UTI. 36 patients (62%) were found to have VUR by VCUG, but only 8 (13%) had abnormal RUS, giving a sensitivity, specificity, and false negative rate of 42%, 91%, and 78%, of RUS for predicting VUR. She concluded that “ultrasonography is unreliable in detecting VUR, renal scarring, or inflammatory change and, alone, is inadequate for investigating UTI in children.” These studies show that RUS is an unreliable screening tool for VUR. The contribution of RUS to the management of the hospitalized child with UTI has been studied. Both Mucci and Maguire^[5] and Alon and Ganapathy^[7] found that routine RUS had a negligible effect on the clinical management of children with simple UTI. Our findings are in accordance with these results. In none of the children did the RUS finding change the management of the patients. Goldman *et al.*^[16] reported similar findings in 45 neonates with UTI. Of 12 patients with abnormal RUS, 4 (33%) had normal VCUG, while of 33 patients with normal RUS, 13 (40%) had VUR on VCUG. However, he found urinary tract abnormalities in 22 of 45 (48%) neonates compared to only 18% in our findings (13 of 71). This discrepancy in results can be partly explained by the patient selection methods, as Goldman *et al.* included children who were suspected of urinary tract abnormalities by intrauterine ultrasound, while we excluded any child with known urinary tract anomalies. In a recently published paper, Hoberman *et al.*^[17] studied 309 children, aged 1–24 months, using RUS, DMSA, and VCUG. They found that the sensitivity of

RUS for detecting VUR on VCUG was 10%, and PPV was 40%. They also reported that the identified abnormalities did not modify management, and concluded that RUS and renal scanning at the time of the acute illness were of limited value. These results are generally in accordance with ours, and we concur with his conclusions. Several issues still remain to be clarified: What is the role of intrauterine ultrasound and does the imaging workup need to be changed according to its findings? Another point in question is the role of DMSA as a screening tool. Since we do not perform DMSA routinely, we cannot address the issue of VCUG versus DMSA based on our own data; however, in light of the growing amount of evidence against DMSA as a screening tool, further studies addressing this issue are needed.

CONCLUSIONS

The present study question the yield of routine RUS in the management of young children with simple UTI. The study concludes that RUS should only be performed in children in whom complications such as renal obstruction or abscess are suspected based on an unfavorable clinical course, or in children in whom VUR has been found, to look for renal structure abnormalities.

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Comparison of the Efficacy of Tamsulosin and Placebo in the Management of Acute Urinary Retention Secondary to Benign Prostatic Hyperplasia Undergoing Trial without Catheter until Definitive Therapy

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Abstract

Introduction: Acute urinary retention (AUR) is one of the most significant, uncomfortable and inconvenient events in the natural history of benign prostatic hyperplasia (BPH). The immediate treatment is bladder decompression using urethral or suprapubic catheterization.

Aim: In this study, the effect of tamsulosin has been evaluated in the temporary management of AUR by increasing the rate of successful trial without catheter (TWOC) until definitive therapy.

Materials and Methods: This prospective randomized study was conducted in tamsulosin Group A/placebo Group B. Patients with AUR after catheterization were given once daily dose of tamsulosin 0.4 mg for 4 days. Placebo group, patients with AUR after catheterizations were given 4 days of vitamin tablets. Success criteria for TWOC; trial without the catheter is considered successful if the patient passes urine more than 100 ml with a PVR of <200 ml either in ultrasonography or actually measured by inserting an interferential therapy.

Results: In Group A, the total success rate of TWOC is 59.5% and the failure rate is 40.5%. In Grade 1 prostate, 11 of 12 had successful TWOC (91.66%) with tamsulosin. The success rate of TWOC in Group B is 32.4%, and TWOC is more successful in patients with Grade 1 prostate (6 of 10).

Conclusion: Prostate size has the statistically significant influence on trial without the catheter. Patients with larger prostate have more chances of failure in the trial without the catheter in both groups. However, tamsulosin increases the success rate of trial without the catheter in patients with the larger prostate.

Key words: Acute urinary retention, Benign prostatic hyperplasia, Management, Tamsulosin, Trial without catheter

INTRODUCTION

Acute urinary retention (AUR) is the most common urological emergency in patients with benign prostatic

hyperplasia (BPH). AUR is defined as the sudden and complete inability to void urine voluntarily despite the presence of urine in the bladder and the desire to urinate. 10% of men in 61–70 years age group and 30% in 71–80 years age group would have AUR in the next 5 years (Curtis *et al.* 2001). AUR is the main indication for 25–30% of the patients undergoing prostatic surgery. The event triggering AUR is not identified in most cases. It is the natural history of BPH that progresses to spontaneous AUR. Sudden sympathetic stimulation causes an acute rise in the smooth muscle tone resulting in urinary retention. Alpha blockers aid in voiding by relaxing the smooth

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muscle tone and relieving obstruction.^[1] Patient quality of life is affected by AUR to the extent that it can be comparable to quality of life impaired by acute renal colic.^[2] AUR is usually managed by immediate catheterization and emptying the bladder followed by trial without catheter (TWOC) with medical therapy or immediate surgery for benign prostatic hypertrophy. Immediate surgery (within few days after AUR) with urinary catheter *in situ* is associated with more complications in the post-operative period. Patients on prolonged catheterization without undergoing surgery have to undergo potential morbidity in the form of bacterial colonization the urinary tract, bacteriuria, fever, and urosepsis with involvement of upper urinary tracts. To date, the first line of treatment in these patients is giving TWOC with a prior administration of an alpha-blocker that should increase the likelihood of success. An initial drained volume of urine <1 L following catheterization of AUR, patients with <60–65 years of age, a precipitated AUR and catheterization for more than 3 days would increase the chance of successful TWOC. Patients undergoing TWOC are later subjected to elective transurethral resection of prostate (TURP) or continue drug therapy in the form of alpha-blockers alone or in combination with 5 α reductase inhibitors (5 α RI). 5 α RIs like dutasteride are added to alpha-blockers if the gland size is above 30 cc to reduce the gland size and risk of AUR.^[3]

Aim

In this study, the effect of tamsulosin has been evaluated in the temporary management of AUR by increasing the rate of successful TWOC until definitive therapy. Successful TWOC helps patient to undergo elective TURP without an indwelling urinary catheter or may continue medical therapy if he opts for medical therapy over surgery depending on the indication.

MATERIALS AND METHODS

This prospective randomized study was conducted in the Department of Urology at tertiary care hospital. Tamsulosin Group A; patients with AUR after catheterization were given once daily dose of tamsulosin 0.4 mg for 4 days. Placebo Group B, patients with AUR after catheterizations were given 4 days of vitamin tablets. Success criteria for TWOC; TWOC is considered successful if the patient passes urine more than 100 ml with a PVR of <200 ml either in ultrasonography (USG) or actually measured by inserting an interferential therapy (IFT).

Inclusion Criteria

Patients with AUR due to benign prostatic enlargement were included in this study.

Exclusion Criteria

AUR due to stricture, carcinoma prostate, carcinoma bladder, hematuria with clot retention, neurogenic causes, in immediate post-operative period (any surgery) and TURP (due to early or late complications of TURP), any other previous surgery in bladder neck or urethra or prostate, AUR due to stone disease, drug-induced AUR, AUR due to trauma, or spinal cord diseases were excluded from the study.

Follow-Up

After 4 doses of tamsulosin/placebo, urinary catheter removed, after patient passing urine. Actual urine passed is measured, and post-void residual is measured using USG or IFT. The patient would be planned for TURP and sent to operation theater without an indwelling catheter or would be given alpha-blockers with or without 5 α RIs depending on the indication.

RESULTS

About 74 patients were selected for the study and randomly allocated in two groups, Group A and Group B, each comprising 37 patients. Following catheterization patients in Group A were given 4 doses tamsulosin 0.4 mg in once daily and 8–12 h after the 4th dose, TWOC given. Group B patients were given vitamin tablets for 4 days, and TWOC given same like Group A. Patients selected for both groups were comparable in terms of age group and prostate size. In age Group 1 comprising patients within 51–60 years, there were 18 patients in total (24.3%). In this group, there were 7 patients in Group A (18.9% within group and 9.5% of total) and 11 patients in Group B (29.7% within group and 14.9% of total). Age Group 2 comprises patients with 61–70 years of age. In this age group, there were 35 patients in total 47.3%. In this age group, there were 16 patients in Group A (43.2% within group and 21.6% of total) and 19 patients in Group B (51.4 % within group and 25.7% of total). In age Group 3 comprising patients within 71–80 years, there were 21 patients (28.4%). In this age group, there were 14 patients in Group A (37.8% within group and 18.9% of total). Age group wise both Groups A and B, patients were comparable and statistically no significant difference among both groups. Of the total 74 patients in the study, 22 patients had Grade 1 prostate (29.7% of total), and 12 patients were in Group A (32.4% within group and 16.2% of total), and 10 patients were in Group B (27% within group and 13.5% of total). 38 patients had Grade 2 prostate (51.4% of total), of which 16 were in Group A (43.2% within group and 21.6% of total) and 22 were in Group B (59.5% within group and 29.7% of total). 14 patients had Grade 3 prostate (18.9% of total), of which 9 were in Group A (24.3% within group

and 12.2% of total) and 5 were in Group B (13.5% within group and 6.8% of total) [Table 3].

There exists a statistical significance between both groups with respect to TWOC. Among the failure patients ($n = 40$), 37.5% ($n = 15$) patients are in Group A. This indicates that the Group A significantly differ from Group B with respect to TWOC [Table 2].

In Group A, the total success rate of TWOC is 59.5%, and the failure rate is 40.5%. Age Group 1 (between 51 and 60 years), 6 of 7 patients had successful TWOC (85.7%). Age Group 2 (between 61 and 70 years), 10 of 16 patients had successful TWOC (62.5%). Age Group 3 (between 71 and 80 years), only 6 of 14 patients had successful TWOC (42.9%) and failure (57.1%) is more (8 out of 14) in this age group.

In patients with Grade 1 prostate, 11 of 12 had successful TWOC (91.66%). In patients with Grade 2 prostate, 9 of 16 had successful TWOC (56.25%). In patients with Grade 3 prostate, only 2 of 9 had successful TWOC (22.22%), i.e., TWOC failure (77.78%) is more in these patients.

The success rate of TWOC in Group B is 32.4%, and TWOC success is uniformly less across all age groups in Group B. Group B patients, TWOC is more successful in patients with Grade 1 prostate (6 of 10). TWOC failure rate is more in patients with Grade 2 prostate (16 of 22) and most in Grade 3 prostate (0 of 5) [Table 3].

Table 1: Prostate size grade

Prostate size grade	Group A	Group B
Grade 1	12	10
Grade 2	16	22
Grade 3	9	5

Table 2: TWOC success comparison between Groups A and B

TWOC	Group A	Group B	P
Success	22	12	0.020
Failure	15	25	

TWOC: Trial without catheter

Table 3: Per-rectal prostate size grade and TWOC success

Prostate size grade	Group A	Group B
Grade 1	11	6
Grade 2	9	6
Grade 3	2	0

TWOC: Trial without catheter

DISCUSSION

Management of AUR in patients with BPH is TWOC. After successful TWOC, as the subsequent risk of AUR is high, the patient may undergo TURP immediately or selectively at a later date. In patients without undergoing any treatment, recurrence of AUR is 70% within 1 week of the first episode.^[4] In the past, AUR was an immediate indication for surgery constituting about 25–30% of TURPs.^[5] For deciding management, spontaneous AUR needs to be differentiated from precipitated AUR. Precipitated AUR is the inability to urinate following a trigger cause. These triggering events may be surgery, anesthesia, or usage of drugs with sympathomimetic or anticholinergic effects, antihistamines. AUR without a trigger factor is categorized as spontaneous. Following an episode of spontaneous AUR, 15% of patients had recurrent AUR, and 75% of these patients underwent surgery. Following an episode of precipitated AUR, only 9% had recurrent AUR, and 26% underwent surgery.^[6] Patients undergoing TURP immediately following AUR had significantly higher rates of complications such as re-catheterization (13.8%), septicemia (1.1%), and shock (0.3%).^[7] They also had more urinary tract infections (UTIs), lower tract symptoms, and higher medical expenses. The morbidity like catheter-associated UTI increased by the presence of an indwelling urinary catheter.^[8] Hence, a trial without the catheter is given to the patient. When TWOC is successful, the patient may undergo surgery electively without catheter-associated morbidity. Alpha-blockers like tamsulosin increase the TWOC success rate. Although alpha-blockers increase the success rate of trial without the catheter, they would not prevent progression of the disease. Patients with significant symptoms of frequency, urgency, voiding symptoms, and a prostate size of more than 30 cc on transrectal US or a PSA level more than 1.5 ng/ml are at high risk of progression of the disease.^[9] For preventing progression of the disease, 5 α RIs are added to alpha blockers. If after taking combination therapy for 3 months there are persistent symptoms of frequency and urgency, antimuscarinics may be added to treat symptoms of overactive bladder.^[9] After a period when 5 α RIs have maximal effect (9 months), alpha-blockers can be withdrawn and patient may be monitored clinically.^[9] If patient is symptomatically better, anticholinergics dose reduction or discontinuation may be attempted and patient may be continued on 5 α RI monotherapy.^[9] If the patient still has frequency, urgency or other voiding symptoms as well as erectile dysfunction, the addition of a daily phosphodiesterase Type 5 inhibitor may be considered.^[9] If medical therapy is not tolerated or does not improve symptoms, surgery is considered. According to AUA guidelines surgery is recommended in patients who complain recurrent gross hematuria of prostatic origin, recurrent UTIs, renal dysfunction secondary to

BPH, vesical stones, lower urinary tract symptoms (LUTS) refractory to other therapies and refractory or recurrent urinary retention. Hence, alpha-blockers are used to increase the TWOC success rate and continued to keep the patient catheter free until he undergoes surgery. The patient may continue alpha-blockers in combination with 5 α RIs or anticholinergics depending on indications or his option for medical therapy. In Lucas *et al.* study, the success rate of TWOC has been increased to 52% and recurrence of AUR significantly reduced by administration of alpha-blocker tamsulosin, when compared with the success rate of 34% in placebo.^[10] In our study, success rate of tamsulosin group is 59.5% when compared with that of placebo group 32.4%. Patients in the placebo group had 3 times more risk for failure of trial without the catheter. In another study by Madhu.S.Agarwal *et al.* in India, following AUR in BPH, TWOC success rate is 70% in patients given tamsulosin, when same is compared with placebo 36%.^[11] This success rate with tamsulosin is high when compared with our study (59.5%). In their study by Hua *et al.*, the success rate of TWOC with tamsulosin following an AUR is 61% when compared with control group 28%.^[12] However, in their study efficacy of treatment was not influenced by the volume of the prostate. In our study, size of the prostate significantly influenced the success rate of TWOC both in tamsulosin and placebo group. In our study, there is the statistically significant difference in TWOC success in patients given tamsulosin concerning prostate size. In patients with Grade 1 prostate, 11 of 12 had successful TWOC (91.66%). In patients with Grade 2 prostate, 9 of 16 had successful TWOC (56.25%). In patients with Grade 3 prostate, only 2 of 9 had successful TWOC (22.22%), i.e., TWOC failure (77.78%) is more in these patients (P -value = 0.005). In MTOPS study also, it was established that efficacy of alpha-blockers was less effective in men with large prostate.^[13] In their study, Fitzpatrick *et al.* found that age more than 70 years, prostate size more than 50 cc, severe LUTS, drained volume at catheterization more than 1000 mL, and spontaneous AUR favored TWOC failure whereas catheterization for more than 3 days and α 1 blockade before TWOC increased success of TWOC.^[14] In our study, in patients given tamsulosin, TWOC success rate in 51–60 years group is (85.7%) more when compared with same (42.9%) in 71–80 years age group, but it is not statistically significant. However, prostate size influenced the TWOC success in both tamsulosin and placebo group, and that is statistically significant. Patients with Grade 3 prostate, TWOC failure is more in both tamsulosin and placebo group, when compared with Grade 1 prostate. These patients had higher TWOC success when given tamsulosin (22.22% vs. 0%). In our study tamsulosin showed a higher success rate of TWOC in patients with larger prostate like Grades 2 and 3 prostates. TWOC success rate in the placebo group is significantly less in these

patients. Hence, use of tamsulosin in patients presenting with AUR, and large prostate increases TWOC success rate. In our study average post-void residual urine after TWOC in patients treated with tamsulosin is 163.51 ml (standard deviation of 103.93) and in the placebo group, post-void residual urine is 212.97 ml (standard deviation of 90.49 ml). This is statistically significant observation. Hence, this study demonstrated that prior administration of tamsulosin significantly reduces post-void residual urine in the trial without the catheter.

CONCLUSION

Tamsulosin increases the success rate of trial without the catheter in patients with AUR. There are 3.056 times odds (risk) for placebo Group B comparative to tamsulosin Group A concerning the failure of trial without the catheter. Prostate size has the statistically significant influence on trial without the catheter. Patients with larger prostate have more chances of failure in the trial without the catheter in both groups. However, tamsulosin increases the success rate of trial without the catheter in patients with the larger prostate. Post-void residual urine is significantly reduced by addition of tamsulosin in patients with AUR undergoing trial without the catheter. Tamsulosin increases the success rate of TWOC in older age group patients with AUR due to BPH compared with placebo. However, this is not statistically significant in our study.

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A Study of the Learning Approaches of Medical Students before and after Clinical Posting in a Medical College in South India

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Abstract

Introduction: Students use either a deep or a surface learning approach focusing on understanding or memorizing, respectively. Learning approaches vary depending on the learning environment, curricula followed and year of study.

Aim: The aim of this study was to compare the learning approaches of medical students before and after they start their clinical posting.

Materials and Methods: The revised two-factor study process questionnaire (R-SPQ-2F) was administered to 93 second-year medical students of Sri Muthukumaran Medical College Hospital and Research Institute aged 19–20 years who were posted in the Departments of General Medicine and Surgery before and after 3 months of their clinical posting. Deep and surface learning approach main scores were determined.

Results: The majority (87.1%) of medical students in our study had a deep learning approach, and there was no change after their clinical posting. There was no significant difference in the deep approach and surface approach main scores and subscale scores before and after their clinical posting. The majority felt that studying was more satisfying (94%), interesting (92%), and exciting (76%) and they felt like working harder (75%) and learning more deeply (82%) because they had seen patients. The majority agreed that after seeing patients, they try to understand concepts (94%), relate new to previous knowledge (84%), logically analyze information (86%), and study out of curiosity (91%) to master the subject (84%).

Conclusion: The majority of medical students had a deep approach to learning before starting their clinical posting and perceived that seeing patients during their clinical posting had a positive effect on their learning, although no statistically significant difference was found in learning approach scores.

Key words: Clinical posting, Learning approach, Medical students, Revised two-factor study process questionnaire

INTRODUCTION

Students have been found to use either a deep or a surface learning approach focusing on understanding or memorizing, respectively.^[1] The choice of preferred

learning approach depends on the learning environment.^[2] Students' learning approaches can be determined using instruments such as the revised two-factor study process questionnaire (R-SPQ-2F).^[1] While students who use a deep learning approach are intrinsically motivated to learn and focus on understanding study material, students who use a surface learning approach memorize facts without understanding them fully. Such students with a surface approach are motivated by fear of failure – their motivation to learn is extrinsic and they aim to just memorize and reproduce study material in examinations. Intrinsically motivated students with deep learning approaches, learn for understanding and mastery, intending to correlate

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new knowledge with existing knowledge, with a focus on application.^[3]

Generally, the aim of our educational systems should be to encourage students to adopt a deep approach to learning subjects crucial for their development.^[3] Medical students too, like all other students, use either deep or surface learning approaches. Researchers have studied the learning approaches of medical students in different years of study intending to determine if there is any change as they progress through medical school. While 1st-year medical students have been found to have low deep approach scores,^[4] a subsequent decline,^[5] or no change^[6] in deep approach scores has also been observed. Other factors have also been found to affect medical students' learning approaches – A deep learning approach has been found to be promoted by a problem-based learning (PBL) curriculum and clinically oriented teaching.^[7,8]

Paudel *et al.* found that medical students in their preclinical (basic science) years of medical education at Trinity School of Medicine adopted the deep learning approach more than the surface approach.^[9] They also found a positive correlation between deep learning approach scores and academic performance.^[9] Sandover *et al.* found a significant and consistent difference between the learning approaches of undergraduate (UG) and Graduate Entry Medical Program (GEMP) students of the University of Western Australia over 5 years (from 2007 to 2011), the GEMP students preferring a deep learning approach and the UG students preferring a superficial learning approach to learning, the difference being more evident in the clinical years.^[10] Recently, Chonker *et al.* who studied the learning approaches of 250 medical students with different backgrounds from various medical schools who attended the obstetrics and gynecology clinical rotation in a hospital at Singapore, found that the majority of students predominantly utilized the deep and strategic learning approaches and that learning approaches were not influenced by demographic characteristics such as age and gender.^[11] A positive correlation between 4th-year medical students' deep learning approaches and performance on a summative high-stakes clinical performance examination has also been noted.^[12]

Generally, medical students in India study basic sciences in their 1st year of study and encounter patients only in their 2nd year. Knowledge of basic sciences provides the basis for medical students' understanding not only of patients' clinical features but also helps them understand the pathogenesis and management of different diseases that patients they subsequently encounter suffer from. Recent reforms in medical education in India have favored and recommended early clinical exposure of medical students by proposing to expose even 1st-year medical

students to patients – either actual or standardized patients or patient videos or paper cases.^[13] In the recent Vision 2015 document, the Medical Council of India (MCI) has recommended various curricular reforms such as early clinical exposure of UG students and student–doctor methods of clinical training so that students understand the relevance and practical application of basic science (Anatomy, Physiology, and Biochemistry) subject matter that they study.^[13] Medical colleges are in different stages of implementing these reforms. Our institution has introduced early clinical exposure. Since some researchers have found that the 1st-year medical students have lower scores on the deep approach when compared to medical students in subsequent years;^[4] theoretically, it is possible that exposure to patients in the hospital (or even early clinical exposure) could promote a deep approach to learning in a short duration. Results could also however vary between different institutions depending on the learning environment.

In view of the varied findings of other researchers regarding learning approaches of medical students in various years of study and the effect of clinically oriented teaching, we were interested in determining the learning approaches of medical students in our institution before they start their clinical posting, with an aim of comparing it with their learning approaches after their clinical posting. The objectives of this study were to compare the percentage of medical students with a deep and surface learning approach, before and after clinical posting and to compare the deep and surface learning approach scores of Indian medical students before and after their clinical posting using the R-SPQ-2F.^[1]

MATERIALS AND METHODS

After obtaining the required Institutional Ethical Committee clearance and written informed consent from the participants, the R-SPQ-2F^[1] was administered to 93 medical students of Sri Muthukumaran Medical College Hospital and Research Institute in Chennai, South India, aged 19–20 years who were posted in the Departments of General Medicine and Surgery before starting their clinical posting and after 3 months of their clinical posting.

The R-SPQ-2F, like the earlier Bigg's SPQ, is used to determine learning approaches of students.^[1] The R-SPQ-2F, which has just surface and deep approaches and a motive and strategy score for each approach is a simple, revised, short two-factor version of the SPQ.^[1] The SPQ scores give information on the student's preferred, ongoing and contextual approaches to learning and give a good idea about the presage, process, and product levels of Bigg's "Presage-Process-Product model" of the learning process – it describes how each student differs within a

particular teaching context; how each student handles a specific task; and how different teaching contexts differ from each other.^[1,14] The R-SPQ-2F has twenty questions, each student was instructed to choose the single best response to each question about their usual way of studying from which deep approach and surface approach main scores and the motive and strategy subscale scores were determined.^[1] A pretested validated questionnaire was also administered after 3 months of their clinical posting to elicit their perceptions about the effect of clinical posting on their learning approaches.

Deep and surface approach scores of the medical students before and after 3 months of clinical exposure were compared using SPSS 17 software and the paired Student's *t*-test; while McNemar's test was used to compare the percentage of medical students with each learning approach before and after their clinical posting.

RESULTS

This study conducted to compare the learning approaches of medical students before and after their clinical posting in a medical college in South India revealed the following results:

The majority (87.1%) of medical students in our study had a deep learning approach, and there was no change after their clinical posting [Table 1]. There was no significant difference in the deep approach and surface approach main scores and the motive and strategy subscale scores of the participants before and after their clinical posting [Table 2].

Analysis of the students' perceptions of the effect of clinical posting on their learning approaches revealed that the majority of students felt that studying was more satisfying (94%), interesting (92%), and exciting (76%) and they felt like working harder (75%) and learning more deeply (82%) because they had seen patients during their clinical posting. The majority agreed that after seeing patients, they try to understand concepts (94%), relate new to previous knowledge (84%), logically analyze information (86%), and study out of curiosity (91%) to master the subject (84%).

DISCUSSION

Our study revealed that the majority (87.1%) of medical students had a deep approach before starting their clinical posting. Our results are contrary to those of Newble and Gordon who studied the learning approaches of 1st, 3rd, and final-year medical students and found that the 1st-year medical students had low scores on the deep approach.^[4] Our results also are in contrast to the results of McDonald *et al.*

Table 1: Comparison of the learning approaches of medical students before and after clinical posting

Learning approach	n=93 (%)		P value
	Before	After	
Deep	81 (87.1)	81 (87.1)	1.00
Surface	8 (8.6)	11 (11.8)	0.581
Equal	4 (4.3)	1 (1.1)	0.375

Learning approaches of medical students before and after 3 months of clinical posting expressed as the number and the percentage (in brackets) of medical students who had a deep or surface learning approach and equal scores for both learning approaches; P value calculated using Mc Nemar's test, P<0.05 being considered significant

Table 2: Comparison of the learning approach scores of medical students before and after clinical posting

Scale	Before	After	P value
DA	32.86±5.41	32.85±5.63	0.985
SA	22.26±6.54	22.50±6.10	0.715
DM	17.12±2.97	16.86±3.28	0.452
DS	15.74±3.28	15.99±3.21	0.515
SM	9.75±3.52	10.29±3.52	0.145
SS	12.51±3.73	12.20±3.45	0.465

Learning approaches scores of medical students before and after 3 months of clinical posting expressed as the means and standard deviations of DA and SA main scores (Max=50) and the DM, DS, SM, and SS subscale scores (Max=25) obtained using the R-SPQ-2F; P value obtained using paired Student's *t*-test, P<0.05 being considered statistically significant. DA: Deep approach, SA: Surface approach, DM: Deep motive, DS: Deep strategy, SM: Surface motive, SS: Surface strategy, R-SPQ-2F: Revised two-factor study process questionnaire

who followed a cohort of students studying Physiology and Anatomy (two of the subjects that our medical students study in their 1st year of study) as their majors for a science degree over 3 years to determine if there was any change in learning approach. They found that a surface approach was predominantly favored by the 1st-year students.^[15] The findings of the present study are in agreement of those of Paudel *et al.* who also found that 1st-year medical students had a deep learning approach.^[9] Our earlier studies however have demonstrated that the majority of 1st-year medical students studying in different Indian medical colleges in which a didactic, nonproblem-based curriculum was followed had a deep approach to learning.^[16,17] The learning approaches of the participants in the present study were determined before they began their clinical posting in their 2nd year, which effectively could be considered being their learning approaches at the end of their 1st year of study, again involving a predominantly didactic, nonproblem-based curriculum, the only difference being the introduction of the curricular reform of early clinical exposure.

The majority of medical students in our study perceived that seeing patients during their clinical posting had a positive effect on their learning, although no statistically significant difference was found in learning approach scores. One possible explanation for this finding could be

the fact that their deep approach scores were already high. This could explain why in spite of a perceived positive effect of the clinical posting, there was no significant further increase in deep learning approach scores. A similar finding was observed by Wilson and Fowler who concluded that students already taking a deep approach do not shift in their approach to deep learning in response to a change in learning environment – they were consistent in their approaches across different environments.^[18]

We can only postulate that the early clinical exposure being practiced in the institution as part of curricular reforms could have accounted for the deep approach scores of the participants. Given the fact that data about the participants' baseline learning approach scores at the start of their 1st year of study were unavailable and given that there were no control groups/cohorts to compare with, this cannot be assumed to be the only cause for the findings, however. Early clinical exposure took the form of paper cases being discussed and patient's videos being shown to students during their course of study in the 1st year and to an extent could have been instrumental in demonstrating relevance of study material and its application which would favor a deep learning approach. However, while some researchers have found that the deep approach to learning was promoted when curricula where PBL and clinically oriented teaching was followed,^[7,8] Reid *et al.*, however, found little significant change and Balasooriya *et al.* found that students moved in the opposite direction and adopted a more surface approach after reforms aiming to promote a deep learning approach were initiated.^[6,19]

Limitations of the study include the fact that results of this study cannot be generalized since the students' approaches would be dependent on the teaching context in each specific institution. The lack of baseline data on the participants learning approaches on entry into medical college, the absence of a control group, the short duration of the study, the self-reporting nature of the questionnaire, and the possibility of social desirability bias are other limitations. Further studies to follow-up the cohort over a longer period and the use of qualitative methods are planned and could provide more information.

CONCLUSION

The majority of medical students had a deep approach to learning before starting their clinical posting and perceived that seeing patients during their clinical posting had a

positive effect on their learning, although no statistically significant difference was found in learning approach scores. Reasons could be their high deep approach scores (possibly due to early clinical exposure) and the short study duration. Lack of baseline data is a limitation. Follow-up after 1 year and focused group discussions are planned.

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Cross-sectional Study of Menstrual Irregularities in Patients Receiving Antipsychotic Medications

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Abstract

background: A significant percentage of women taking antipsychotic medication may be suffering from menstrual irregularities during their treatment.

Aims: This study was aimed at studying the relationship between the use of antipsychotic medication and type frequency of menstrual irregularities in women of reproductive age group.

Setting: Psychiatric outpatient department (OPD) in general hospital.

Materials and Methods: The study of women of reproductive age group on neuroleptic medications attending the psychiatric OPD was questioned about the menstrual pattern, duration of treatment along with diagnosis, current medications, and age.

Results: A total of 96 patients were enrolled in the study after taking informed consent. 48.95% patients showed menstrual irregularities. Among those patients who had menstrual irregularities, 35% had amenorrhea, and 65% suffered from oligomenorrhea. Among the medications, equal frequency was seen between atypical and typical antipsychotic medications.

Conclusion: A substantial proportion of the patients on antipsychotic medications suffers from menstrual irregularities. The patients, hence, need to be explained about these side effects and the psychiatrist should actively lookout for these symptoms as the majority are not reported. It is believed that typical antipsychotics have more side effects compared to atypicals, but when it came to menstrual irregularities, we found equal prevalence between the two groups.

Key words: Amenorrhea, Antipsychotics, Menstruation, Neuroleptics

INTRODUCTION

Menstrual irregularities are among the most neglected of the side effects in the patients receiving antipsychotics medications.^[1] Relative frequency of the patients reporting these irregularities varies from 18% to 75%.^[1] Majority of the studies are carried in western population, and hence, data pertaining to the Indian population

largely remains obscure. The significance of studying menstrual irregularities lies in the fact that it serves as a marker for serum prolactin and elevated prolactin levels are associated with adverse effects on multiple systems in the body, namely menstrual irregularities in women,^[2,3] galactorrhea,^[2,4] sexual dysfunction,^[5] and osteoporosis.^[6,7,8]

Aims and Objectives

The objectives of this study are as follows:

1. To study the prevalence of menstrual irregularities in women of reproductive age group receiving antipsychotic medications.
2. To compare the relative frequency of menstrual irregularities in patients receiving typical and atypical antipsychotics.

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MATERIALS AND METHODS

Inclusion Criterion

The following criteria are included in the study:

1. All the patients willing to participate in the study and giving informed consent.
2. All the women in reproductive age group (15–45 years) receiving antipsychotics for at least 2-month duration.
3. All patients receiving single antipsychotic drug (monotherapy).

Exclusion Criterion

The following criteria are excluded from the study:

1. All patients unable to give information due to underlying psychiatric illness or any other reason.
2. All patients suffering from medical or neurological condition likely to affect menstruation.
3. Patients on multiple or on combination of antipsychotic drugs.

Procedure

Each patient in the current sample when came to psychiatric outpatient department was interviewed with set of questions regarding details of menstrual pattern, antipsychotic medications currently taking, total duration of treatment, and diagnosis. Amenorrhea was defined as the absence of menstruation for 6 consecutive months, and oligomenorrhea was defined as menstrual cycle lasting for more than 35 days.

Statistical Analysis

All the collected data were tabulated and analyzed using appropriate statistical methods.

RESULTS

All 96 patients who followed within 12 months were enrolled in the study. The mean age of the patients was 32.14 years (range 17–46). Total 47 (48.95% \pm 5% absolute precision) of 96 patients showed menstrual irregularities. Among those patients who had menstrual irregularities, 16 (34.04%) had amenorrhea, which was defined as the absence of menstruation for a consecutive period of 6 months and 31 (65.95%) suffered from oligomenorrhea, which was defined as menstrual cycle lasting for more than 35 days. Majority of the patients had the diagnosis of schizophrenia 63 (65.62%), while 15 (15.62%) had bipolar mood disorder and 18 (18.75%) had diagnosis of other psychiatric disorders.

Table 1 summarizes all the patients receiving single medication from all age groups and shows that maximum patients were from 25 to 35 age group.^[9]

Table 2 summarizes all the patients who are distributed according to disease. Patients receiving single medication show that maximum patients were from schizophrenia but with equal frequencies of oligomenorrhea and amenorrhea. The frequency of oligomenorrhea was 67.7% and 70% for schizophrenia and bipolar mood disorder, respectively.^[9] Similarly, the relative frequency of amenorrhea was 32.2% and 30% for schizophrenia and bipolar mood disorder, respectively.^[9]

Table 3 summarizes the patients who were exclusively on the first-generation antipsychotics and the second-generation antipsychotics. The frequency of oligomenorrhea was 66.6% and 33.3% for the first-generation and second-generation antipsychotics, respectively.^[9] Similarly, the relative frequency of amenorrhea was 64.3% and 35.71% for the first-generation and second-generation antipsychotics, respectively.^[9]

DISCUSSION

In the available literature, around 30–40% of the patients suffer from menstrual irregularities when receiving antipsychotics medications.^[10] Results found in our study are in congruence with the previous studies in this respect. Among menstrual irregularities, oligomenorrhea was found to be more common than amenorrhea.

Contrary to popular belief that typical antipsychotics have greater propensity to cause menstrual side effects compared to atypical antipsychotics,^[11] we found equal incidence between the two groups. Although clozapine is considered to have less side effects in terms of menstrual disturbances.^[12] Menstrual irregularities are secondary to raised prolactin levels and as measuring serum prolactin is

Table 1: Age wise distribution

Age	n (%)			
	Total	Oligomenorrhea	Amenorrhea	Normal
Up to 25 years	29 (30.2)	09 (64.28)	5 (35.71)	15 (51.72)
25–35 years	34 (35.45)	10 (62.5)	6 (37.5)	18 (52.94)
35–45 years	33 (34.3)	10 (62.5)	6 (37.5)	17 (51.51)

Table 2: Disease wise distribution

Disease	n (%)			
	Total	Oligomenorrhea	Amenorrhea	Normal
Schizophrenia	64 (66.66)	21 (67.74)	10 (32.25)	33 (51.56)
Bipolar mood disorder	21 (21.87)	7 (70)	3 (30)	11 (52.38)

Table 3: Type wise distribution

Type of neuroleptics	n (%)			
	Total	Normal menstruation	Oligomenorrhea	Amenorrhea
First-generation antipsychotics	39 (40.62)	21 (53.84)	12 (66.66)	6 (33.33)
Second-generation antipsychotics	57 (59.37)	29 (50.87)	18 (64.28)	10 (35.71)

expensive, menstrual irregularities are gateway for raised prolactin.

The intervention which could be tried includes decreasing the dose of the antipsychotic, switching to another medication with less effect on prolactin, or using a dopamine agonist, for example, bromocriptine or amantadine.^[13,9]

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A Randomized Comparative Study on Bispectral Index Monitoring on Early Postoperative Recovery in Morbidly Obese Patients Undergoing Laparoscopic Sleeve Gastrectomy

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Abstract

Introduction: Obesity has become a relatively common condition that has a tendency to profoundly affect morbidity and mortality. With an increase in the prevalence of obesity, the anaesthesiologists are challenged with these population of patients posted for surgery due to various medical and surgical pathologies.

Objective: The objective of this study was to evaluate the role of bispectral index (BIS) monitoring in recovery time in obese patients undergoing laparoscopic sleeve gastrectomy.

Materials and Methods: A total of 80 patients of both sex aged between 25 and 45 years, posted for laparoscopic sleeve gastrectomy were randomized into two groups of 40 each (Group 1 – BIS and Group 2 – non-BIS group) using computer randomization. Time taken for recovery from anesthesia as noted by the mean time taken for awakening and the mean time taken for extubation along with the mean time to achieve a modified Aldrete score of ≥ 9 were recorded in minutes.

Results: Between Groups 1 and Group 2, the mean awakening time (11.38 ± 2.807 and 14.92 ± 3.885 with $P = 0.000$), mean extubation time (15.90 ± 2.863 and 19.28 ± 4.120 with $P = 0.000$), and mean time to achieve modified Aldrete score ≥ 9 were (31.60 ± 3.862 and 40.80 ± 4.681 with $P = 0.000$), respectively. There was a statistically significant difference between the two groups in awakening time, extubation time, and modified Aldrete score.

Conclusion: The present study had revealed that using BIS monitoring lead to early postoperative recovery of morbidly obese patients undergoing laparoscopic sleeve gastrectomy.

Key words: Bispectral index, Modified aldrete score, Obesity, Sleeve gastrectomy

INTRODUCTION

The word obesity is derived from the Latin word *obesus* meaning fattened by eating. Obesity has been become a relatively common condition that has a tendency to

profoundly affect morbidity and mortality. According to the WHO, obesity is defined by calculating body mass index (BMI) or Quetelet Index. BMI of 18–24.9 is normal, 25–29.9 is overweight, 30–34.9 is Grade I obesity, 35–39.9 is Grade II Obesity, and >40 is morbid obesity (WHO 1997) [1,2]. Obesity is a major risk factor for many chronic diseases such as diabetes, hypertension, coronary artery disease, high triglycerides and cholesterol, sleep apnoea, strokes, gallbladder disease, and carcinomas.

With this increase in the incidence of obesity, there is an increased incidence of a wide range of medical and surgical pathologies and an anesthesia providers are challenged with

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these populations of obese indiv^[3,4] Obesity predisposes to several potential problems to the patient in the perioperative period such cardiovascular and respiratory events and also challenges anesthesiologists providing difficult mask ventilation and laryngoscopy.^[5,6] Conventionally, obesity has been seen as a physiologic state that magnifies the importance of the fat–blood solubility coefficient of the anesthetic in its relation to emergence and recovery; hence, early and uneventful postoperative recovery of morbidly obese patients remains a challenge for anesthesiologists. All volatile anesthetics accumulate over time in adipose tissue delaying recovery from anesthesia. Obesity magnifies the importance of the fat–blood solubility coefficient of the anesthetic in its relation to emergence and recovery.^[7]

In obese patients, factors such as decrease total body water, increase in adipose tissue, altered tissue protein binding, increase in renal blood flow, and glomerular filtration rate all lead to alteration in pharmacokinetics of the drug in comparison to nonobese patient. Hence, monitoring precise endpoint of anesthesia is important in preventing undue delay in recovery, reducing postoperative morbidity, and complications. Clinical studies involving electroencephalographic-based cerebral monitors have demonstrated titration of both intravenous^[8,9] and inhalational^[10,11] anesthetics during general anesthesia. Bispectral index (BIS) monitoring is a form of electroencephalography-based cerebral monitor that uses bispectral analysis and has been proven to be effective in preventing awareness [Figure 1]. Bispectral analysis is a statistical technique that allows the study of phenomena with nonlinear character, such as surf beats and wave breaking.^[12] Bispectral analysis provides a description to a continuous pseudorandomly varying signal (e.g., electroencephalogram [EEG]) that is an alternative to other conventional power spectral analysis techniques derived from fast Fourier transformation. The EEG information, from which the BIS value is derived, is obtained by placing the sensor on the patient's forehead connecting it to the patient interface cable. The sensor transmits EEG signal to the monitor where it is processed through a complex and sophisticated algorithm, resulting in a BIS value which provides information on patient's status. BIS is a dimensionless number scaled from 100–0, with 100 representing an awake EEG and zero representing complete electrical silence (cortical suppression) [Figure 2]. In nonobese patients, optimizing anesthesia level using BIS monitoring will probably help shorten recovery time and reduce total anesthetic drug consumption.^[10,11,13] However, it could be even more valuable to titrate the administration of some inhaled anesthetic, such as sevoflurane, in morbid obese patients, the hypothesis being to shorten emergence from anesthesia using BIS monitoring. It would be a great advantage if BIS permitted a more rapid recovery.

The aim of this randomized comparative study was to investigate the effect of BIS monitoring on extubation and recovery times, in morbidly obese patients undergoing laparoscopic sleeve gastrectomy under general anesthesia using desflurane as maintenance anesthesia.

MATERIALS AND METHODS

This study was conducted in the Apollo Hospital, Chennai in December 2013–December 2014 after the ethics committee approval. A total of 80 morbidly obese patients (BMI >40 kg/m² and BMI >35 kg/m² or more and experiencing obesity-related health conditions, such as high blood pressure [BP] or diabetes) belonging to the American Society of Anesthesiologists (ASA) physical status 1 or 2 between the age groups of 25 and 45 years and scheduled for elective laparoscopic sleeve gastrectomy were included in the study. Informed and written consent



Figure 1: The bispectral index module

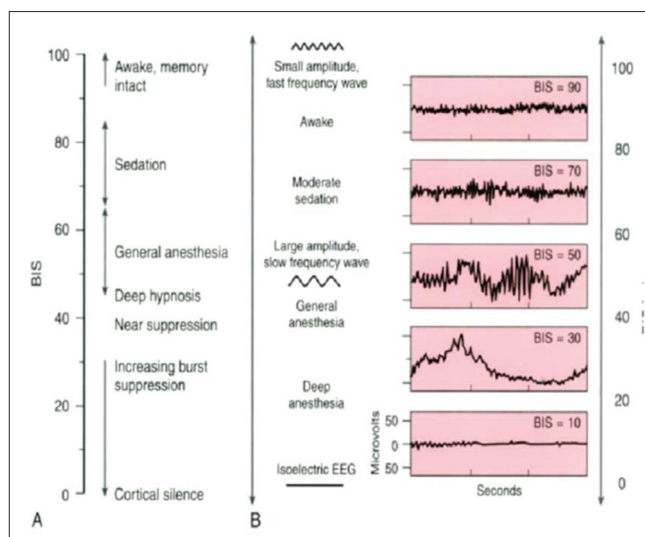


Figure 2: Clinical correlation of bispectral index

was obtained from each patient. Each patient underwent a preoperative evaluation and advised nil by mouth for 6 h.

Patients were randomly allocated into two groups (40 patients each) as follows: Group 1 (40 patients) were anesthetized with the use of BIS (BIS Group). Group 2 (40 patients) were anesthetized without the use of BIS (Non-BIS Group).

All the patients were premedicated with pantoprazole 40 mg orally at the night before surgery and metoclopramide 10 mg orally with sips of water 3 h before surgery. Basal vital parameters were recorded and patient preloaded with ringer's lactate solution. Following preoxygenation, intravenous induction was done with injection fentanyl 2 µ/kg and injection propofol 1.5–2 mg/kg. Intravenous rocuronium 0.9 mg/kg was administered to facilitates tracheal intubation and neuromuscular blockade. All patients were mechanically ventilated with 40% oxygen mixed with air to maintain an end-tidal carbon dioxide concentration of 35–40 mmHg and desflurane 6%. Intravenous paracetamol 1 g was given to all patients of both groups over 20 min after induction of anesthesia and local infiltration with bupivacaine 0.25% was given by the surgeon before all skin incisions. BIS monitoring (BISA-2000 software 2.21, Aspect Medical Systems, Newton, MA, USA) was initiated at induction, and smoothing time was 30 s (only in BIS group). Desflurane 6% in 2 L/min fresh gas flow, mixed in air and oxygen, was administered to all patients after endotracheal intubation until skin incision, then the concentration was changed every 5 min as follows:

In non-BIS group, the desflurane concentration was adjusted purely according to the clinical signs (heart rate [HR] and BP).

In BIS Group, anesthesiologists adjust the desflurane concentration to achieve a target BIS in the range of 40–60. During the surgery, the patients in both groups were observed for signs of inadequate anesthesia (increased BP and HR 20% from baseline, lacrimation). Significant hypotension or bradycardia was defined as 20% reduction of vitals from their baseline. Any instances of inadequate anesthesia were managed by increasing the concentration of desflurane. Rocuronium 0.15 mg/kg neuromuscular blockade was maintained to a single twitch of train of four. During the past 15 min of surgery in the BIS group, desflurane was titrated to maintain BIS in the range of 60–70. Neuromuscular blockade was reversed with neostigmine 0.07 mg/kg and glycopyrrolate 0.015 mg/kg intravenously. A verbal command to open eyes was given every 30 s. After a train-of-four ratio higher than 0.9 and a 5 s, head lift was performed by the patients, patients were extubated.

Time from discontinuation of inhalational agent (Desflurane) to the eye opening and extubation and recovery times (eye opening on verbal commands and orientation to the time place and person) were assessed at 1 min interval and documented.

After extubation, when the patients were full awake, patients were transferred to post anesthetic care unit (PACU) with oxygen 4 L/min using oxygen mask. All patients were observed in PACU for 3 h. Postoperative pain was evaluated with five-point verbal rating scale for pain. Postoperative pain was treated with injection ketoprofen 100 mg intramuscularly. Time to attain modified Aldrete score ≥ 9 [Figure 3] was recorded by PACU nurse in minutes (min).

RESULTS

Based on the previous study, the sample size was calculated as 40 in each group. The sample size of 80 is enough to maintain the power of study at least 80%. All the continuous variables were assessed for the normality using Shapiro–Wilk's test. If the variables were normally distributed, they were expressed as the mean \pm standard deviation, otherwise median (interquartile range). All the categorical variables were expressed either as percentage or proportions. Comparison of normally distributed continuous variables was done by either independent sample *t*-test or ANOVA based on the number of groups. Comparison of non-normally distributed continuous variables was being done by Mann–Whitney U-test or Kruskal–Wallis H test. Comparison of categorical variables was done by either Chi-square test or Fishers exact test based on the number of observations. Data entry was done in MS-Excel spread sheet. Data validation and analysis were carried out using SPSS Version 11.0. All $P < 0.05$ were considered as statistically significant. Majority of patients in our study was female accounting 56.2% of the total. There were no

Parameter	Description of patient	Score
Activity level	Moves all extremities voluntarily/on command	2
	Moves 2 extremities	1
	Cannot move extremities	0
Respirations	Breathes deeply and coughs freely	2
	Is dyspneic, with shallow, limited breathing	1
	Is apneic	0
Circulation (blood pressure)	Is 20 mm Hg > preanesthetic level	2
	Is 20 to 50 mm Hg > preanesthetic level	1
	Is 50 mm Hg > preanesthetic level	0
Consciousness	Is fully awake	2
	Is arousable on calling	1
	Is not responding	0
Oxygen saturation as determined by pulse oximetry	Has level >90% when breathing room air	2
	Requires supplemental oxygen to maintain level >90%	1
	Has level <90% with oxygen supplementation	0
Maximum total score is 10; a score of ≥ 9 is required for discharge.		

Figure 3: Modified Aldrete score

significant differences between males and females in relation to BIS values at various stages of anesthesia. As mentioned in [Table 1 and 2], the mean age in BIS group was 34.3 ± 5.33 year, and the mean age group in non-BIS group was 35.5 ± 5.90 . There was no statistically significant difference ($P = 0.378$) when comparing age between BIS group and non-BIS group. The mean BMI in BIS group is 46.1 kg/m^2 and in non-BIS group is 44.9 kg/m^2 (P value of BMI-0.496). The mean BMI difference was not statistically significant between two groups. The mean HR was calculated for BIS and non-BIS group and was found to be 77.8 ± 3.39 and 79.1 ± 3.4 . There was no statistically significant difference between two groups ($P = 0.095$). The mean MAP was calculated for BIS and non-BIS group and was found to be 94.5 ± 3.5 and 95.8 ± 4.2 . There was no statistically significant difference between two groups ($P = 0.136$). The mean awakening time in minutes, extubation time in minutes, and time to achieve modified Aldrete score ≥ 9 were compared between two groups and were found to be mean awakening time (BIS 11.38 ± 2.807 and non-BIS 14.92 ± 3.885 with $P = 0.000$) [Graph 1], mean extubation time (BIS 15.90 ± 2.863 and non-BIS 19.28 ± 4.120 with $P = 0.000$) [Graph 2], and mean time to achieve modified Aldrete score (BIS 31.60 ± 3.862 and non-BIS 40.80 ± 4.681 with $P = 0.000$) [Graph 3]. There was a statistically significant difference between the two groups in awakening time ($P = 0.000$), extubation time ($P = 0.000$), and modified Aldrete score ($P = 0.000$).

DISCUSSION

In this study, we compared the effects of BIS monitoring on early postoperative recovery in morbidly obese patients

undergoing laparoscopic sleeve gastrectomy. In this study, we found that there were no statistical differences in intraoperative mean arterial BP and mean HR in both groups. There were statistically significant differences in awakening time, extubation time, and time to achieve modified Aldrete score ≥ 9 .

Similarly, Punjasawadwong *et al.*^[14] results demonstrated that BIS reduced the recovery times; time for eye opening in 2557 patients was 1.93 min, response to verbal command in 777 patients was 2.73 min, time to extubation in 1501 patients was 2.62 min, and time to orientation in 373 patients was 3.06 min, and Song *et al.*^[10] have shown that titrating desflurane and sevoflurane using BIS monitor decreased the utilization of those volatile agents and contributed to a faster emergence from anesthesia in outpatients undergoing laparoscopic tubal ligation procedures.

Klopman *et al.*^[15] showed that BIS monitoring results in early recovery, shorter stays in the ICU, and reduced drug costs similar to our study. Results similar to our study were also observed by Boztug *et al.*^[16] who studied the effects of BIS monitoring in 50 ASA physical status I-II patients posted for craniotomy. At the end of the study, recovery times as defined as time for the first spontaneous breathing, eye opening, and extubation ($P = 0.035$, $P = 0.001$, and $P = 0.0001$) were significantly shorter in BIS group. Ekman *et al.*^[17] in their study, reported that the use of BIS monitoring during general anesthesia requiring endotracheal intubation and/or muscle relaxants was associated with a significantly reduced incidence of

Table 1: Demographic data and intraoperative, postanesthetic data for the BIS group and non-BIS group

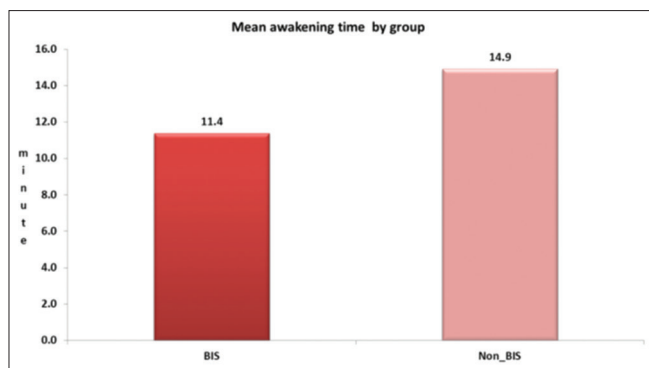
Data	BIS group <i>n</i> =40	Non-BIS group <i>n</i> =40	<i>P</i> value
Gender M/F	19/21	16/24	0.652
Age in year	34.3 ± 5.33	35.5 ± 5.90	0.378
ASA I and II	19/21	16/24	0.652
BMI kg/m^2	46.115 ± 7.35	44.917 ± 8.28	0.4906
Mean intraoperative HR	77.8 ± 3.39	79.1 ± 3.4	0.095
Mean intraoperative blood pressure (mm Hg)	94.5 ± 3.5	95.8 ± 4.2	0.136

BIS: Bispectral index, ASA: American Society of Anesthesiologists, BMI: Body mass index, HR: Heart rate

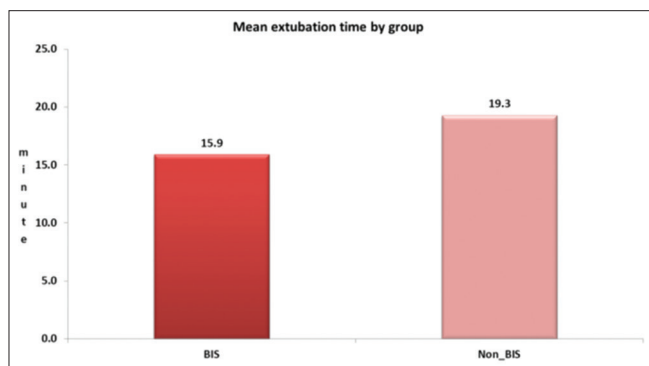
Table 2: Awakening time, extubation time, and time to achieve

Data	Group	Number	Mean (min)	Std. deviation	<i>P</i> value
Awake time	BIS	40	11.38	2.807	0.000
	Non BIS	40	14.92	3.885	
Extubation time	BIS	40	15.90	2.863	0.000
	Non BIS	40	19.28	4.120	
Time to achieve modified Aldrete score ≥ 9	BIS	40	31.60	3.862	0.000
	Non BIS	40	40.80	4.681	

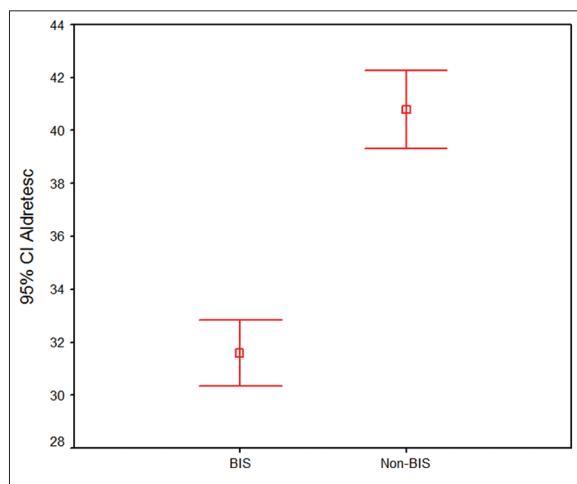
Aldrete score ≥ 9 in min expressed as mean \pm SD in minutes. SD: Standard deviation, BIS: Bispectral index



Graph 1: Bar diagram showing the difference in awakening time in min between the two groups



Graph 2: Bar diagram showing the difference in extubation time in min between the two groups



Graph 3: Error bar diagram showing the difference in attaining the modified Aldrete score ≥ 9 in min between the two groups

awareness. Heavner *et al.*^[18] had demonstrated that the use of BIS monitoring had improved recovery profiles in elderly patients anesthetized by desflurane and nitrous oxide. White *et al.*^[19] found that AEP and BIS monitoring can decrease the end-tidal desflurane concentration during maintenance of anesthesia and discharge times after the end of anesthesia.

The present study had demonstrated that using BIS monitoring lead to early postoperative recovery of morbidly obese patients undergoing laparoscopic sleeve gastrectomy. There was a significant difference in recovery times when comparing BIS-guided and non-BIS-guided anesthesia. The results were compared to those reported in other studies that assessed titration of propofol,^[20] desflurane, or sevoflurane^[10,21] by using BIS monitoring, but not in morbidly obese patients. Song *et al.*^[9] had concluded that BIS monitoring allows reduction in the total amount of intraoperative anesthetic consumption and appears to decrease emergency and recovery times. In this study, there were significant differences in the times of eye opening to verbal commands, extubation time, and orientation to time, place, and person between BIS and non-BIS groups. However, there were no statistically significant differences between mean HR and mean arterial blood pressure between two groups.

The use of cerebral monitors to minimize the intraoperative anesthetic drug consumption and improve the recovery process had raised concerns regarding the potentially deleterious effects of increased autonomic activity (e.g., myocardial ischemia) as well as the possibility of intraoperative awareness. However, in this study, intraoperative hemodynamic variables were not statistically significant.

CONCLUSIONS

The use of BIS monitoring was effective in reducing the recovery times in morbidly obese patients posted for elective laparoscopic sleeve gastrectomy. The difficult recovery and extubation in morbidly obese patients will be made ease with the use of BIS intraoperatively without compromising the hemodynamics and patient outcome. BIS monitoring clearly has a function in improving safety during sedation; however, anesthesiologists need to be proactive in providing rational guidelines for conscious sedation with or without BIS and improving patient safety. Depending on the specific patient characteristics, surgical procedure, and planned anesthetic technique, utilization of BIS monitoring may be a very appropriate decision.

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Study of Lipid Profile Changes in Cirrhosis of Liver

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Abstract

Introduction: Cirrhosis is defined anatomically as a diffuse process with fibrosis and nodule formation. It is the result of the fibrogenesis that occurs with chronic liver injury. For reduced liver biosynthesis capacity, low level of triglyceride and cholesterol is usually observed in the chronic liver disease. Due to the high prevalence of chronic liver disease in our country we have conducted this study to determine lipid profile in a patient with cirrhosis and to assess its relationship to the severity of cirrhosis.

Purpose of Study: The purpose of this study was to study the serum lipid profile changes in liver cirrhosis patients in comparison to age- and sex-matched apparently healthy control patients and to find the significance of lipid abnormalities in liver cirrhosis patients with the severity of cirrhosis of the liver.

Materials and Methods: The present study had been carried out in the Department of Medicine, Medical College and associated Hospital, Jabalpur (Madhya Pradesh) India, from March 2016 to August 2017. This was a case-control observational study. The targeted populations were 75 of cases with liver cirrhosis and age- and sex-matched 75 apparently healthy control patients.

Results: There was a significant decrease in serum high-density lipoprotein (HDL), low-density lipoprotein (LDL), triglyceride, very low-density lipoprotein (VLDL), and total cholesterol in cases as compared to controls. Of 75 cases, one (1.30%) was belonging to Child-Turcotte-Pugh (CTP) Class A, 34 (45.30%) to Class B, and 40 (53.30%) to Class C. All lipid profile parameters were decreased more in CTP-C compared to CTP-B.

Conclusion: We have concluded that there was a significant decrease in serum total cholesterol, LDL cholesterol, VLDL cholesterol, HDL cholesterol, and serum triglyceride level in liver cirrhosis patients which belongs to the Child-Pugh Class C.

Key words: Cholesterol, Cirrhosis, Fibrosis, Lipid, Nodule

INTRODUCTION

Cirrhosis is defined anatomically as a diffuse process with fibrosis and nodule formation. It is the result of the fibrogenesis that occurs with chronic liver injury.^[1]

Previous studies have been observed that in Western countries, the prevalence of alcoholic cirrhosis, nonalcoholic

steatohepatitis (NASH) cirrhosis, and viral cirrhosis in particular hepatitis C, are all increasing. In developing countries, such as India the predominant causes for liver cirrhosis were found due to infection from hepatitis virus B and C; however, alcohol and autoimmune condition may be in increasing trends.^[1]

Lipoproteins are complexes of lipid and proteins that are essential for transport of cholesterol, triglycerides, and fat-soluble vitamins. As we know, that the liver is the principal site of formation and clearance of lipoproteins; hence, liver disorders can affect plasma lipid level in a variety of ways. Hepatitis due to infection, drugs, or alcohol is often associated with increased very low-density lipoprotein (VLDL) synthesis and mild-to-moderate hypertriglyceridemia. Severe hepatitis and liver failure

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such as cirrhosis are associated with dramatic reductions in plasma cholesterol and triglycerides due to reduced lipoprotein biosynthetic capacity.^[2]

As there is increasing prevalence of chronic liver diseases in the form of cirrhosis in our country, we have been conducted this study in our tertiary care hospital to determine the lipid profile changes in cirrhotic patients in comparison to age- and sex-matched apparently healthy control patients and also assess its correlation with severity of liver cirrhosis irrespective to its etiologies.

MATERIALS AND METHODS

Place of Study

The present study had been carried out in the Department of Medicine, Netaji Subhash Chandra Bose Medical College and Hospital, Jabalpur, in the state of Madhya Pradesh, India, between the periods of March 2016 and August 2017.

Type of Study

The present study was a case–control observational study.

Aims and Objectives of Study

The primary objective of the present study was to assess the serum lipid profile changes in liver cirrhosis patients (cases) and its comparison to age- and sex-matched apparently healthy control population.

The secondary objective was to find the significance of lipid abnormalities in cirrhotic patients (cases) with the severity of cirrhosis of liver.

Inclusion Criteria

Irrespective of the etiologies, 75 liver cirrhosis patients were taken as cases and 75 apparently healthy age- and sex-matched patients as controls. The case and control patients were selected from the indoor of Medical Wards, Medical Out Patients Department, relatives of the cases, and volunteers from the institution, respectively. Both case and control patients were belong to ≥ 18 – ≤ 80 years of age groups of both sexes.

Laboratory Tests

All the relevant investigations have been done in the Department of Pathology, Radiology, and Cardiology of Netaji Subhash Chandra Bose Medical College and Hospital, Jabalpur, Madhya Pradesh. Some test results were obtained from the National Institute for Research in Tribal Health (I.C.M.R.), Jabalpur. The fasting blood samples have been collected from all study patients for lipid profile study.

Lipid profile test was performed using the Randox RX Imola fully automated biochemistry analyzer machine.

The diagnosis of liver cirrhosis was performed on the basis of typical signs and symptoms of the disease which have been further confirmed by detailed physical and clinical examinations along with the abdominal ultrasound imaging study and biochemical liver panel known as liver function tests which included mainly alanine aminotransferase and aspartate aminotransferase (ALT and AST), prothrombin time, serum bilirubin, albumin, and total serum proteins. The serological tests (hepatitis B surface antigen and antihepatitis C virus [HCV]) were also used to support the diagnosis of viral infections. Whenever needed cardiac 2D echocardiography, color Doppler portal vein study, upper gastrointestinal endoscopy, and ascitic fluid examination has also been done accordingly.

The classification of plasma lipid level was done by the criteria adopted from the third report of the National Cholesterol Education Program Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel-III).^[3]

Child-Pugh score (or the Child-Turcotte-Pugh [CTP] score or Child criteria) was used to assess the prognosis and severity of chronic liver disease, mainly cirrhosis.^[4]

Grading of hepatic encephalopathy was done according to practice guideline by the European Association for the study of the liver and the American Association for the study of liver diseases.^[5]

Exclusion Criteria

The patients were using insulin or other hypoglycemic drugs and/or cholesterol-lowering medicines within the previous 30 days. Patients with a history of other medical illnesses which may influence the serum lipid level such as diabetes mellitus, hypertension, chronic smoker, nephrotic syndrome, and/or thyroid dysfunctions were excluded from the study.

Statistical Analyses

The present study was a case–control observation study. The study data have been recorded by using structured schedule (Case Report Form) and entered for tabulation in Microsoft Excel Sheet. Statistical data were analyzed using STATA 12.1 (Stata Corp LP) TX, USA software. Chi-square test was used for the comparison of frequency and percentage distribution in cases and controls. Student t-test was applied to compare mean and standard deviation (SD) of difference between cases and controls. Level of statistical significance was calculated with *P* value (<0.05 significance) consideration.

RESULTS

In the present study, it is summarized that total $n = 75$ patients with liver cirrhosis of both sexes have been taken as cases irrespective of the etiology of liver cirrhosis and $n' = 75$ of age- and sex-matched apparently healthy patients were taken as controls after fulfillments of their inclusions and exclusions criteria.

In the present study, the age of the liver cirrhosis patients (cases) ranged from ≥ 18 years to ≤ 80 years of age with the mean age of 43.47 and SD 14.12 years. The age distributions in control group were also ranged from ≥ 18 years to ≤ 80 years of age with the mean age of 43.21 and SD 14.47. The observed P value was 0.914, which found statistically nonsignificant; hence, both study groups were comparable in terms of age [Table 1].

Of total $n = 75$ cases of liver cirrhosis, the present study groups were comprised $n = 56/75$, (74.66%) of male and $n = 19/75$, (25.33%) of female patients (cases) and from total $n' = 75$ control patients $n' = 17/75$, (22.70%) were found female and $n' = 58/75$, (77.30%) male.

The maximum numbers of cases were observed with alcoholic etiology, i.e., $n = 42/75$, (56.2%) followed by hepatitis B, $n = 11/75$, (14.6%) and hepatitis C, $n = 2/75$, (2.6%). The remaining liver cirrhosis cases were diagnosed with etiology as others, which comprised $n = 20/75$, (26.6%) of cases [Table 2].

Serum level of total cholesterol, high-density lipoprotein (HDL), serum triglycerides, and VLDL cholesterol were observed significantly low in cases compared to apparently healthy control patients ($P = -0.0001$, statistically highly significant) [Table 3].

Of total number of $n = 75$ patients in case group, $n = 1/75$, (1.30%) belong to CTP Classification Class A, $n = 34/75$, (45.53%) of cases belong to CTP Class B, and $n = 40/75$, (53.30%) belong to CTP Class C [Table 4].

Serum total cholesterol and HDL level decreased more in CTP Class C as compared to CTP Class B ($P = 0.03$ found statistical significance); which can be further correlated with the severity of cirrhosis. In the present study, the level of low-density lipoprotein (LDL), serum triglycerides, and VLDL were observed low in cases belongs to the CTP Class C in comparison to CTP Class B patients (P value found statistically nonsignificant) [Table 5 and Graph 1].

Of $n = 75$ patients (cases) with liver cirrhosis, the maximum number of cases was belongs to the model for end-stage liver disease (MELD) score 10–19, i.e., $n = 46/75$, (61.31%)

and minimum number of cases $n = 05/75$, (6.7%) have MELD score < 10 .

In the present study, we have observed that the cases have total serum proteins level relatively very low from controls serum proteins value (P value found statistically significant).

DISCUSSION

After observation of data and results, following discussion was made:

In the present study, we have been observed that the mean value of age distribution in cases was 43.47 ± 14.12 years and 43.21 ± 14.47 years in control patients, respectively. The P value was 0.914 which found statistically nonsignificant in both groups; hence, both groups were comparable in terms of age. The maximum numbers of cases, i.e., 23

Table 1: Age-wise distribution of cases and controls

Age group (in years)	Number (%)	
	Cases ($n=75$)	Controls ($n'=75$)
>18–28	10 (13.33)	13 (17.33)
29–39	23 (30.67)	19 (25.33)
40–50	22 (29.33)	24 (32.00)
51–60	12 (16.00)	10 (13.33)
61–70	5 (6.67)	6 (8.00)
71<80	3 (4.00)	3 (4.00)
Total	75 (100)	75 (100)

n =Number of patients (cases), n' =Number of patients (controls)

Table 2: Distribution of cases according to primary etiology of liver cirrhosis

Primary etiology of liver cirrhosis	Frequency of cases $n=75$ (%)
Alcoholic	42 (56.2)
HBV	11 (14.6)
HCV	2 (2.6)
Others	20 (26.6)
Total	75 (100)

n =Number of patients (cases). HBV: Hepatitis B virus, HCV: Hepatitis C virus

Table 3: Comparison of lipid profile with cases and controls

Parameters (mg/dl)	Mean \pm SD		Statistical analysis	
	Case ($n=75$)	Control ($n'=75$)	t test	P value
S. total cholesterol	135.33 \pm 37.04	172.79 \pm 26	7.17	0.0001
HDL	31.99 \pm 7.85	43.11 \pm 7.85	8.68	0.0001
LDL	79.58 \pm 23.13	112.27 \pm 22.8	8.72	0.0001
Serum triglyceride	88.1 \pm 37.92	151 \pm 40.84	10.18	0.0001
VLDL	20.11 \pm 10.74	27.28 \pm 9.06	4.92	0.0001

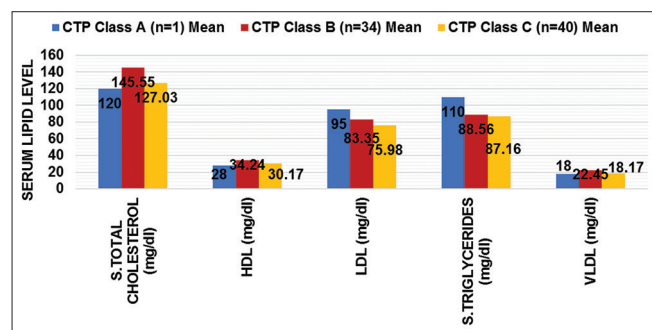
n =Number of patients (cases), n' =Number of patients (controls). SD: Standard deviation, HDL: High-density lipoprotein, LDL: Low-density lipoprotein, VLDL: Very low-density lipoprotein

(30.67%) were belong to 29–39 years of age group and the maximum numbers of control patients, i.e., 24 (32%) were belong to 40–50 years of age group.

Muhammed *et al.*^[6] have been observed in their study that the majority numbers of patients were belong to the age of 51–60 years (39.8%). If consider the age-wise distributions of cases and controls, the results of the above study were found not relevant to the present study.

Phukan *et al.*^[7] have been included the total number of $n = 100$ patients as cases and $n = 50$ noncirrhotic, nonalcoholic individuals as control patients in their study. They have also been found in their study that the most common affected age group was 41–50 years (41%). The above study data for the age group were found relevant to the present study.

In the present study, of total number of cases ($n = 75$), males were belong to $n = 56/75$, (74.66%) and female $n = 19/75$, (25.33%). The total number of control patients in our study was ($n' = 75$) from which $n' = 58/75$, (77.3%) were found male and $n' = 17/75$, (22.7%) female.



Graph 1: Comparison of Child-Turcotte Pugh-Class with serum lipid profile status of cases

Table 4: Case distribution according to CTP classification and scoring system

Child-Pugh Class (CTP)	No. of cases belongs to CTP $n = 75$ (%)
A	1 (1.30)
B	34 (45.30)
C	40 (53.30)

n =Number of cases. CTP: Child-Turcotte-Pugh

Table 5: Comparison of CTP class with serum lipid profile status of cases

CTP class	Mean \pm SD			Significance	
	A ($n = 1$)	B ($n = 34$)	C ($n = 40$)	t-test	P value
Serum total cholesterol (mg/dl)	120 \pm *	145.55 \pm 44.48	127.03 \pm 27.6	2.19	0.03
HDL (mg/dl)	28 \pm *	34.24 \pm 8.21	30.17 \pm 7.19	2.27	0.03
LDL (mg/dl)	95 \pm *	83.35 \pm 21.81	75.98 \pm 24.11	1.37	0.17
S. triglycerides (mg/dl)	110 \pm *	88.56 \pm 44.91	87.16 \pm 24.36	0.17	0.86
VLDL (mg/dl)	18 \pm *	22.45 \pm 14.54	18.17 \pm 5.58	1.72	0.09

*Only single patient was belongs to CTP Class A so that it could not be analyzed statistically. n = Number of cases (patients) out of total 75 cases. HDL: High-density lipoprotein, LDL: Low-density lipoprotein, VLDL: Very low-density lipoprotein, CTP: Child-Turcotte-Pugh

The present study was done by Nangliya *et al.*^[8] have been observed in their study that of 150 clinically diagnosed patients of cirrhosis (cases); 66% males and 34% females were included in the study, and results were compared to the age- and sex-matched 50 normal healthy control patients.

Mandal *et al.*^[9] have been studies of total 120 cirrhotic patients as cases from which 80 were male and 40 female patients.

In the present study, we have taken $n = 75$ cases and $n' = 75$ control patients, which was a low sample size. Hence, the present study results may vary for sex distribution (in percentage) from the above-described study results; however, the overall male patients were found more in all above-mentioned studies as described in our study results also.

In the present study, it was observed that the maximum number of cases have alcoholic etiology $n = 42/75$, (56.2%) which followed by hepatitis B; $n = 11/75$, (14.61%) and least have hepatitis C $n = 2/75$, (2.6%).

In the present study, the etiology of liver cirrhosis that belongs to the category of others causes was comprised $n = 20/75$, (26.6%) of cases.

Verma *et al.*^[10] have been observed that the maximum number of patients with liver cirrhosis have hepatitis B virus-(HBV) related cirrhosis $n = 55/139$, (39.57%) which followed by other etiologies $n = 39/139$, (28.05%); alcohol $n = 34/139$, (24.46%); and HCV-related cirrhosis $n = 11/139$, (7.9%), respectively.

Nangliya *et al.*^[8] have been observed in their study that the main etiologic cause for liver cirrhosis from 150 cirrhotic patients was the alcohol (42.6%) followed by HBV (20.7%), NASH (20%), other (10%), and HCV (6.7%), respectively.

The explanation of this difference was that the demographic variation may vary the study result for cirrhosis etiology.

In this study, we have observed that the value of serum total cholesterol, HDL, LDL, serum triglyceride, and VLDL

was significantly low in cases compared to healthy control patients ($P = 0.001$ found statistically highly significant).

Mandal *et al.*^[9] have been observed in their study that in patients with chronic liver diseases, with the exception of triglyceride level, there was a significant decrease in total cholesterol, LDL cholesterol, VLDL, and HDL cholesterol levels compared to the control group ($P < 0.05$ found statistically highly significant).

Kumar *et al.*^[11] have been observed in their study that the level of serum cholesterol, LDL, HDL, and VLDL cholesterol in cases was significantly reduced when compared to control group ($P < 0.000$). They have also been observed that the levels of triglyceride were marginally reduced in cases ($P < 0.05$).

Nangliya *et al.*^[8] study result has showed that all the serum lipid profile parameters (total cholesterol, LDL, and HDL) were significantly ($P < 0.05$) decreased in cirrhosis as compared to control group and the concentration of these study variables decreased with the severity of liver disease. They were also observed in their study that the triglyceride levels rather showed a decline in cirrhotic patients; however, it was not statistically significance.

Phukan *et al.*^[7] have found in their study result that in patients with cirrhosis, the total serum cholesterol level was decreased. There was a significant decrease in serum HDL and LDL cholesterol compared to the control group ($P < 0.001$). However, serum triglyceride level was significantly increased in alcoholic cirrhosis patients compared to the control group ($P < 0.001$).

Ghadir *et al.*^[12] have found in their study results that in patients with liver cirrhosis, there was a significant decrease in serum triglyceride, total cholesterol, LDL cholesterol, and HDL cholesterol levels compared to the comparison group (mean of 82 vs. 187, 138 vs. 184, 80 vs. 137, and 40 vs. 44 mg/dl, respectively); all $P < 0.05$ found statistically significant. They have also concluded that the comparison of lipid profile with the pathologic progression of liver cirrhosis revealed that except for serum triglyceride level, other serum lipids diminish linearly with the progression of liver damage. The probable explanation for the reduced serum total cholesterol in liver cirrhosis patients was due to the decline in synthetic function and altered metabolism.

The overall emphasis of above-mentioned studies results were comparable with present study results in terms of serum lipid profile status in patients of liver cirrhosis (cases), and age- and sex-matched apparently healthy controls except the few variable results for serum

triglycerides value that might be due to more or less severity and/or progression of liver disease status.

In the present study, the serum level of total bilirubin was observed (mean 4.61, SD 4.47), serum glutamate-pyruvate transaminase (SGPT)/ALT (mean 57.47, SD 61.08), and serum glutamic-oxaloacetic transaminase (SGOT)/AST (mean 100.91, SD 102.91) in cases which were found significantly higher in comparison to controls, i.e., total serum bilirubin (mean 0.85, SD 0.32), SGPT/ALT (mean 31.44, SD 12.83), and SGOT/AST (mean 33.69, SD 13.76), respectively ($P = 0.0001$, found statistically highly significant).

Kumar *et al.*^[11] have been described that the routine liver function tests, i.e., serum bilirubin, SGPT used in the assessment of liver function may give abnormal results in various kind of liver disorders, and furthermore, these tests reflect the extent of hepatic cell damage, rather than hepatic function assessment which is more important to evaluate the patient's condition and progression. They were observed in their study that serum total bilirubin, (mean 4.44, SD 2.86 in cases and mean 0.59, SD 0.33 in controls), and SGPT (mean 74.58, SD 28.21 in cases and mean 26.85, SD 8.38 in controls). The statistical analysis has showed that the unpaired *t*-test was 13.36, $P < 0.000$ and 16.21, $P < 0.000$ for total serum bilirubin and SGPT, respectively, which is comparable with present study results.

In the present study, the maximum numbers of cases were belong to CTP Class C group, i.e., 40 (53.30%) and minimum numbers of cases were belong to CTP Class A group, i.e., 1 (1.30%).

In the present study, it was observed that the only single patient (case) was belongs to CTP Class A; hence, it was not included in statistical analysis.

Kumar *et al.*^[11] have been observed that the reduction in the LDL cholesterol level was proportionate to the severity of liver damage in cirrhosis as detected by the Child-Pugh scoring system. In their study, they have included 100 cases of liver cirrhosis from which according to CTP classification belong to Class A - 18, Class B - 33, and Class C - 49 of cases, respectively. Their study results have showed that patients with liver diseases had lower lipid level, i.e., lower LDL in cirrhotic patients than in the comparison group. Besides, the amount of decrement in the serum LDL was significant with increasing severity of liver damage.

Nangliya *et al.*^[8] study result has showed that all the serum lipid profile parameters (Total cholesterol, LDL, and HDL) were significantly ($P < 0.05$) decreased in cirrhosis

as compared to control group and the concentration of these study variables decreased with the severity of liver disease. They were also observed in their study that the triglyceride levels rather showed a decline in cirrhotic patients; however, it was not statistically significant. They have concluded in their study that the serum lipid level decreases progressively with the severity of liver disease and assessment of plasma lipid and lipoprotein levels will be helpful to evaluate the extent of the hepatic damage. They have further concluded that the hypolipidemia is a common finding in chronic liver disease and has got the significant association with the Child-Pugh class so that it may increase the reliability of Child-Pugh classification in assessment of severity and prognosis in chronic liver disease patients.

Ghadir *et al.*^[12] have observed in their study that according to Child-Pugh classification criteria, 11 (22%) of patients had score "A," 14 (28%) score "B," and 25 (50%) had score "C" from total 50 patients. They have also observed that there was a significant ($P < 0.05$) negative correlation between liver damage according to child criteria and serum total, HDL, and LDL cholesterol level ($P < 0.05$) so that more severe the liver damage is, the more decline in lipid level is detected, especially in LDL and total cholesterol levels. However, they were found no correlation between the serum triglyceride level and the extent of liver damage.

In the present study, the maximum number of patients (cases) belongs to 10–19 MELD score, i.e., 46 (61.3%).

Ghadir *et al.*^[12] have observed in their study that according to MELD criteria of 50 patients, 10 patients had MELD scores <10 , 15 had MELD scores between 11 and 18, 17 had MELD scores between 19 and 24, and 8 had MELD scores >25 . Further, they have observed that there was a significant ($P < 0.05$) negative correlation between liver damage according to MELD score and serum total, HDL, and LDL cholesterol level ($P < 0.05$).

In the present study, it was observed that the serum total cholesterol and HDL levels were low in patients belong to CTP Class C in comparison to patients belong to CTP Class B; ($P = 0.03$, found statistically significant).

In the present study, the level of LDL, serum triglycerides, and VLDL was observed low in cases which belong to CTP Class C in comparison to cases belongs to CTP Class B (P value statistically not significant).

In the present study, the Child-Pugh Class A was recorded in a single patient so that there it was not included in statistical analysis.

Mohammed *et al.*^[6] in their cross-sectional study of total 170 consecutive chronic liver disease patients which were analyzed over 1 year, it was observed that among the total 170 patients, 24 patients belong to CTP score Class A, 47 patients were in Class B, and 52 patients were in Class C. Hence, they have observed a significant ($P < 0.001$) negative correlation of all the lipid profile parameters with the severity of liver disease.

Kumar *et al.*^[11] have observed that the levels of serum lipid included triglyceride, LDL, HDL, and total cholesterol in cases were significantly reduced in child score C compared to B and compared to A, i.e., decrease in lipids was proportional to the child class. They have also observed in their study that there was no significant variation in the VLDL levels in all the child classes.

Nangliya *et al.*^[8] in their analytical cross-sectional study of 150 cirrhotic patients of their sex ranging in the age from 25 to 65 years were included in the study, and the results were compared to 50 age- and sex-matched healthy control patients. They had observed that when all cirrhotic patients were assessed for severity of disease as mild (Child A), moderate (child B), and severe (child C) as per Child-Pugh classification along with the serum total cholesterol, HDL, LDL, and triglyceride measurement, the results of the study showed that all the serum lipid profile parameters (which included total cholesterol, LDL, and HDL) were significantly ($P < 0.05$) decreased in cirrhotic patients as compared to control group and the concentration of these study variables decreased with the severity of liver disease and the mean level difference was statistically significant ($P < 0.01$) with the exception of serum triglyceride levels. Triglyceride levels rather showed a decline in cirrhotic patients; however, it was not statistically significant. So that, they have concluded that dyslipidemia exists in patients with liver cirrhosis and serum lipid profile is routinely measured parameter which may have independent prognostic value in patients with liver cirrhosis. Thus, the assessment of the serum lipid profile is important for effective treatment and prognostic evaluation of patients with the chronic liver disease.

Mandal *et al.*^[9] have resulted that in patients with chronic liver diseases with the exception of triglyceride level, there was a significant decrease in total cholesterol, LDL cholesterol, VLDL, and HDL cholesterol levels compared to the control group ($P < 0.05$). However, they have observed no significant correlation between severity of cirrhosis and change in serum lipid levels.

In the present study, we were observed that the cases have total serum protein (mean 6.27, SD 0.86), serum albumin (mean 2.66, SD 0.72), and serum globulin (mean 3.60,

SD 0.80) mg/dl, respectively, which were compatibly very low from controls serum proteins value, i.e., total serum proteins (mean 6.87, SD 0.57), serum albumin (mean 4.05, SD 0.49), and serum globulin (mean 2.81, SD 0.55) mg/dl, respectively ($P = 0.0001$, found statistically significant).

CONCLUSION

After analyzing the data and results finally we are concluded that as follows:

1. In the present study, there was a significant decrease in serum total cholesterol, LDL cholesterol, VLDL cholesterol, HDL cholesterol, and serum triglyceride levels in liver cirrhosis patients (cases) compared to control patients.
2. The majority of patients (cases) belongs to the CTP Class C, i.e., 40, (53.30%) cases, and least belong to the Class A, i.e., 1 (1.30%) of total 75.
3. In this study, all lipid profile parameters were found decreased in liver cirrhosis patients, which mean dyslipidemia exists in patients with liver cirrhosis and it also further correlated with the severity of liver cirrhosis because we have studied that the CTP Class C group's patients have lowest serum lipid level as compared to CTP Class B patients.

However, further studies are needed to assess the predictive value of dyslipidemia as a tool to forecast the progression of cirrhosis.

LIMITATION OF STUDY

Due to the limitation of resources liver biopsy could not be performed in the patients. On account of financial constraints, several laboratory investigations could not be done as a result of which etiology of cirrhosis in several patients could not find. Gender-wise correlation with outcome could not be done as the numbers of female cirrhotic were very low for comparison. Any result data if found statistical insignificance in the present study was probably attributable to small cohort

under study. This was a single-center study with our limited resources.

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High-Resolution Computed Tomography Evaluation of Lung Parenchymal Changes in Symptomatic HIV-Seropositive Individuals

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Abstract

Introduction: Pulmonary diseases are the leading cause of morbidity and mortality, and one of the frequent cause of hospital admission in HIV-infected people worldwide. High-resolution computed tomography (HRCT) is a very sensitive tool for accurate assessment and characterization of diffuse lung diseases.

Purpose: The purpose of this study is to characterize pulmonary diseases in HIV-seropositive patients presenting with the chest complaints using HRCT and to correlate the radiological findings with a CD4 count of the patient.

Materials and Methods: The study was conducted on 61 HIV-seropositive patients from February 2016 to September 2017 presented with chest symptoms on 128-slice SIEMENS somatom AS definition machine. Computed tomography-guided biopsy and bronchoalveolar lavage were performed in few cases.

Results: Maximum number of patients was in the age group 20–40 years (64%). Out of 61 patients, 43 (70%) were male, and 18 (30%) were female. In our series of 61 patients, 33 (54%) patients were diagnosed as having pulmonary tuberculosis (TB) followed by fungal infection in 9.8% of the patients and interstitial lung disease in 6.5% patients. Bacterial pneumonia, bronchiolitis obliterans, Kaposi sarcoma, and pulmonary thromboembolism were found in 1.6% of patients each. Sensitivity and specificity to detect pulmonary TB by HRCT were found to be 96.5% and 84.3%, respectively.

Conclusion: HRCT is a very sensitive tool for detection and characterization of lung parenchymal changes that help clinicians develop a focussed approach in patient management.

Key words: High-resolution computed tomography, Human immunodeficiency virus, Interstitial lung disease, Pulmonary tuberculosis, Pneumocystis jiroveci pneumonia

INTRODUCTION

About 36.7 million people worldwide are suffering from HIV infection and associated complications.^[1] An estimated 2.12 million people in India are living with HIV infection.^[2]

HIV infection causes an alteration in several lines of host defenses in the lung and respiratory tract that contribute to an increased risk for lung complications. An incidence of 20–25 episodes per 100 hospital admissions per year has been observed.^[3] Many well-described infectious diseases, cancers, and other pulmonary diseases occur with increased frequency in this population. The majority of the pulmonary complications of HIV-positive patients are infectious in origin which depends mainly on the CD4 count, different disease spectrum is seen at a different range of CD4 count of the patient.^[4,5] With the introduction of highly active antiretroviral therapy, survival of HIV-positive patients has also increased and thus the

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range of pulmonary manifestations. All of these factors underscore the importance of understanding pulmonary diseases in HIV-infected patients and of developing a practical approach for chest imaging studies.

The risk of developing tuberculosis (TB) is estimated to be between 16 and 27 times greater in people living with HIV than among those without HIV infection. In 2015, there were an estimated 10.4 million cases of TB disease globally, including 1.2 million (11%) among people living with HIV. Almost 60% (57%) of TB cases among people living with HIV were not diagnosed or treated, resulting in 390,000 TB-related deaths among people living with HIV in 2015.^[6]

Conventional radiography has low sensitivity and specificity and at many times does not lead to a conclusive diagnosis. HRCT of lung provides detailed visualization of lung parenchyma and can characterize diseases according to pattern and distribution which can help in formulating a differential diagnosis.^[7,8] Hence, my study is intended to document these radiological findings and correlate them with patient's CD4 counts.

MATERIALS AND METHODS

This prospective observational study was conducted in the Department of Radio-Diagnosis, Pt. Jawahar Lal Nehru Memorial Medical College and Dr. B.R.A.M. Hospital, Raipur (Chhattisgarh), between February 2016 and September 2017 on 61 HIV-seropositive patients who presented with chest complaints.

A thorough clinical history of all the HIV-positive patients presenting with pulmonary disease was taken. Duration of symptoms was also recorded. Then, a meticulous record of all the available laboratory investigations including HIV status, CD4 counts, routine blood examination, sputum examinations, pleural fluid analysis, and other available investigations was kept. Chest X-rays (CXR) of the patients were studied for the presence of any abnormality.

HRCT scans of the chest were performed on 128-slice SIEMENS somatom definition AS machine.

HRCT Imaging Protocol

The procedure and objectives of performing the high-resolution computed tomography (CT) scan were explained to the patient, and written consent of patient was taken. The patient was explained and demonstrated the procedure of breath holding during the acquisition of HRCT scans.

The patient was kept supine on the gantry table and was scanned cephalocaudal in the axial axis. Scans obtained

with patients supine were adequate in most instances. The scanogram or tomogram was first taken, and then the whole lung was scanned from apex to the base. The scans were performed on 128-slice SIEMENS CT scanner using the following protocol.

Collimation = 1 mm

Feed = 10 mm

KVp = 120–140

mA = 250

Pitch = 6

High-spatial-frequency algorithm was used. It reduces image smoothening and increases spatial resolution and making structures appear sharper. Thus, small vessels and bronchi are better seen in HRCT.

Statistical Methods

Data were expressed as a percentage and mean \pm standard deviation Kolmogorov–Smirnov analysis was performed for checking the linearity of the data. Student's *t*-test correlation analysis was used to check the difference between two parameters in parametric data. Fischer's exact test or Chi-square test was used to analyze the significance of the difference between frequency distribution of the data. ROC curve was plotted for prognostic significance. Correlation analysis was performed using Pearson's correlation. $P < 0.05$ was considered as statistically significant. Microsoft® Inc. USA was used to perform the statistical analysis.

RESULTS

The number of patients included in this study was 61. A maximum number of patients was in the age group 20–30 and 31–40 year. About 64% of patients were 20–40 year old, and only 6% were more than 60-year-old. Out of 61 patients, 70.5% were male, and 29.5% were females. The ratio of male-to-female was 2.3:1.

Maximum 54% HIV patients presented with TB followed by 9.8% fungal infection (including pneumocystis jiroveci pneumonia [PJP], cryptococcosis). Usual interstitial pneumonia (UIP) pneumonia was noted in 6.5% cases (including bronchiolitis obliterans organizing pneumonia [BOOP] and UIP). Bacterial pneumonia, bronchiolitis obliterans, Kaposi sarcoma, and pulmonary thromboembolism were noted in 1.6% cases each. However, 18% of study participants did not reveal any significant abnormality.

Maximum 47.5% patients were having CD4 count in the range of 200–499 cells/mm³ and nearly 34.4% patients have CD4 count <200 cell/mm³.

Out of 100, 63.9% maximum number of patients was identified to have airspace nodules followed by lymphadenopathy in 57.4% cases while 42.6% of patients were identified to have consolidation.

Variable size cavitations were found in 13.1% of patients. Ground-glass opacity and lung cyst were evident in 19.7% and 6.5% of patients, respectively.

Pleural effusion was found in 26.3% of patients, and bronchiectasis was noted in 31.1% of patients.

In our study, among pulmonary TB patients, maximum 84% patients demonstrated airspace nodules followed by lymphadenopathy (75.7%), consolidation (51.5%), pleural effusion (33.3%), bronchiectasis (24.2%), cavitation (21.2%), and ground-glass opacity (18.2%). Cavitation and bronchiectasis were found to be more frequent in TB patients.

Lobar consolidation was seen more in bacterial pneumonia patients. However, diffuse ground-glass opacity and lung cyst were found to be a more consistent feature in PJP patients.

The sensitivity and specificity to detect pulmonary TB by HRCT were found to be 96.5% and 84.3%, respectively.

We compared the CD4 counts with different outcomes (i.e., death, deterioration, and improvement on follow-up). The mean CD4 count was found to be lower in patients with death, poor treatment responders, and the highest with clinical symptomatic improvement; however, the difference failed to reach statistical significance ($P < 0.0001$).

Prognostic significance of CD4 count was demonstrated using ROC curves in which 66.9% area comes under the curve with a sensitivity and specificity 72.5% and 62.5%, respectively.

DISCUSSION

The descriptive study of “HRCT evaluation of lung parenchymal changes in symptomatic HIV-seropositive individuals” was conducted in the Department of Radiodiagnosis, Pt. Jawahar Lal Nehru Memorial Medical College and associated Dr B.R. Ambedkar Memorial Hospital, Raipur (Chhattisgarh), from February 2016-September 2017 on 61 HIV-seropositive patients who presented with the chief complaints of chest symptoms of various age groups. Most of the diagnosis was made on the radiological basis along with clinical and laboratory investigations available. Bronchoscopic lavage and CT-guided lung biopsy were performed in a small number of cases.

A maximum number of patients was in the age group 20–40 years (64%) [Figure 1]. Out of 61 patients

included in our study, 43 (70%) were male, and 18 (30%) were female. Male-to-female ratio was 2.3:1 [Figure 2].

Out of 61 cases in the study, 47.5% patient's CD4 count was in the range of 200–499, and about 34.4% patient's CD4 count was below 200 cells/mm³ [Figure 3].

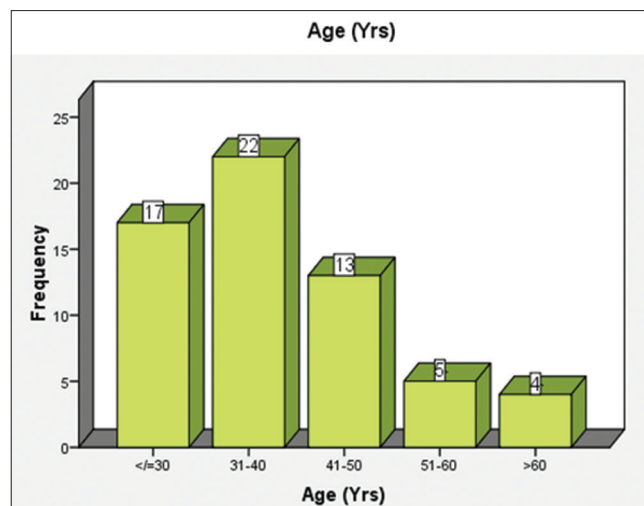


Figure 1: Distribution of HIV-positive patients according to age

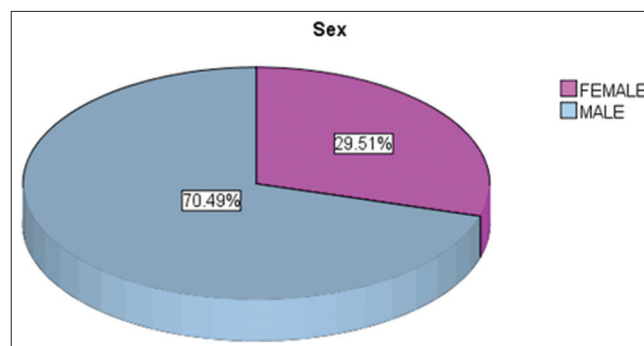


Figure 2: Distribution of HIV-positive patients according to gender

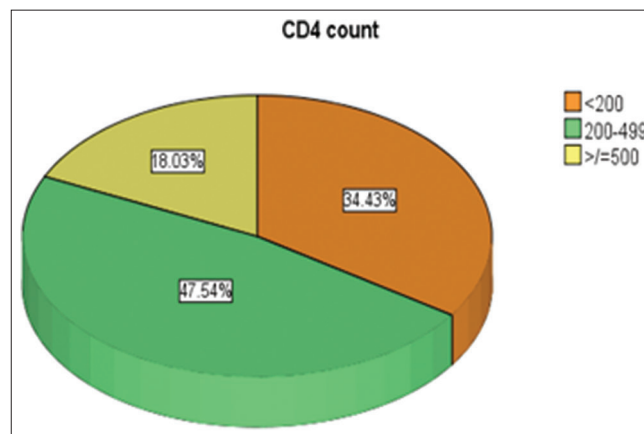


Figure 3: Distribution of HIV-positive patients according to CD4 count

Spectrum of Pulmonary Diseases Noted in Our Study

In our series of 61 patients, about 33 (54%) patients were diagnosed as having pulmonary TB followed by fungal infection (including PJP and cryptococcosis) in 9.8% of the patients, and interstitial lung disease (including BOOP, UIP) in 6.5% patients, while 18% of participants did not reveal any significant abnormality.

Bacterial pneumonia, bronchiolitis obliterans, Kaposi sarcoma, and pulmonary thromboembolism were found in 1.6% of patients each. However, in 4.9% of patients results were inconclusive [Figure 4].

Pulmonary TB

A total of 33 (54%) patients in our study were diagnosed to be suffering from pulmonary TB. The CD4 count in these patients ranged from 74 to 423 cells/mm³. About 12 patients had CD4 count <200 cells/mm³. Different HRCT pattern and their frequency obtained were tabulated in Table 1.

Maximum number (54%) of patients with pulmonary TB were identified to have nodular opacities which were similar to the study conducted by Naseem *et al.*, in which nodules were found in maximum 92% cases.^[9]

Nodules were absent in our five patients. Nodules with cavitations noted in six cases. The centrilobular pattern of distribution was detected in 60.6% of patients, and it was associated with “tree-in-bud” pattern in 55% of cases [Figure 5]. The miliary pattern was evident only in 12.1% of cases [Table 2 and Figure 6].

Lymphadenopathy was noted in 25 (75.7%) cases which is similar to the study conducted by Feng *et al.*, in which the presence of lymphadenopathy was a significant finding (77.2% cases).^[10] Size of the lymph nodes was <1 cm in

14 cases, >1 cm in 11 cases. On contrast administration, seven cases showed peripheral rim enhancement with low-attenuation center suggestive of caseating necrosis due to tubercular infection.

Consolidation was found in 17 (51.5%) cases. Lobar as well as diffusely distributed patches of consolidation were noted among patients.

Cavitation was found in 7 (21.2%) cases. Most of the cavities are located in the upper lung lobes. All the patients having cavitation had CD4 count >200 cells/mm³.

About 11 cases had pleural effusion. Empyema and variable degree lung collapse was noted in three and four cases, respectively.

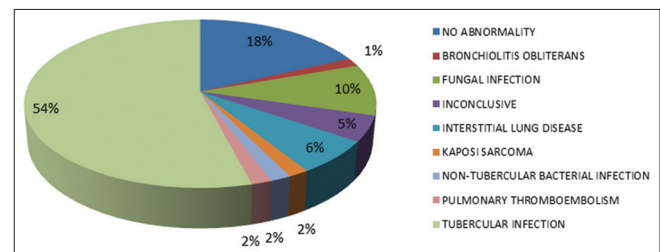


Figure 4: Distribution of HIV-positive patients according to radiological diagnosis

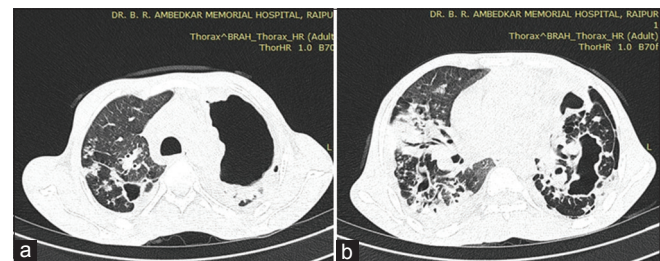


Figure 5: Axial high-resolution computed tomography image at the level of (a) arch of aorta showing multiple centrilobular nodules with clustering and tree-in-bud pattern at some places. Thick-walled cavitory lesion is also seen at the left upper lobe. (b) Airspace consolidation with irregular cavitory lesion noted involving bilateral lower lobes. Case of culture-positive pulmonary tuberculosis

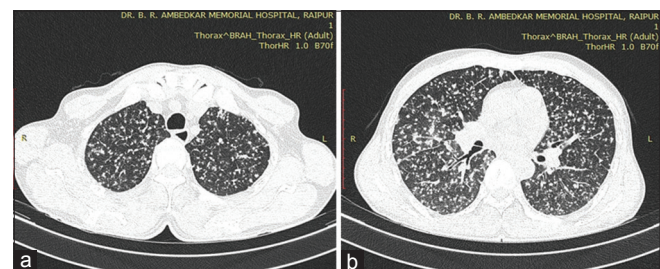


Figure 6: Axial high-resolution computed tomography images (a) through the upper lobes (b) subcarinal level showing miliary nodules diffusely involving bilateral lung fields. Case of miliary tuberculosis

Table 1: HRCT patterns and their frequency in pulmonary tuberculosis cases

HRCT findings	No. of patients (%)
Nodules	28 (84.8)
Lymphadenopathy	
Present	25 (75.7)
<1 cm	14 (56)
>1 cm	11 (44)
Necrotic	7 (28)
Consolidation	17 (51.5)
Cavitation	7 (21.2)
Ground-glass opacity	6 (18.2)
Pleural effusion	11 (33.3)
Empyema	3 (9.1)
Collapse	4 (12.1)
Bronchiectasis	8 (24.2)
Pleural thickening	3 (9.1)
Emphysema	3 (9.1)

HRCT: High-resolution computed tomography

Bronchiectasis was noted in 24.2% of cases of pulmonary TB.

In a 17 year study conducted in Shanghai, China, pulmonary TB was found to be the main cause of bronchiectasis (13.17%).^[11]

Fungal infection

A total of six patients in our study were diagnosed to have fungal infection.

PJP

A total of three patients were diagnosed to be suffering from PJP. The diagnosis was made on the basis of HRCT findings that were later confirmed on bronchoalveolar lavage findings.

In our study, diffuse ground-glass opacity with intralobular and interlobular septal thickening (crazy paving) is seen in all the cases of PJP pneumonia which is fairly correlated with the study of Tasaka *et al.*^[12] Few tiny lung cysts were also noted in all patients [Figure 7]. All the patients were in severe immunocompromised stage with CD4 counts <200 cells/mm³.

Benito *et al.*, reported that HRCT has a high sensitivity for primary cryptococcal pneumonia (100%) and a specificity of 89%.^[13]

Cryptococcosis

Two cases in our study were diagnosed as cryptococcosis. Subpleural nodules were noted in both the patient, one of them showing cavitation [Figure 8]. Both of the cases have CD4 count <100 cells/mm³. Additional magnetic resonance imaging brain studies revealed enlarged perivascular spaces suggesting diagnosis of cryptococcosis.

Aspergillosis

One case was diagnosed as angioinvasive aspergillosis showing characteristic halo sign on HRCT scan, i.e., multiple pulmonary nodules surrounded by ground-glass opacity [Figure 9].

Interstitial lung disease

A total of four cases showed an interstitial pattern of lung disease in our study participants.

UIP

Two cases of UIP was diagnosed in our case study. Diffuse ground-glass opacity with interlobular and intralobular septal thickening was noted predominantly involving bilateral posterior and lower lung zones with honeycombing, and bronchiectasis noted in one patient, centriacinar emphysematous changes along with a large bulla also noted, while in another patient, ground-glass opacity with reticular opacities, consolidation, and bronchiectasis was noted involving posterobasal segment. Their CD4 counts were 403 and 213 cells/mm³, respectively [Figures 10 and 11].

BOOP

Two cases in our study were diagnosed to have BOOP. Patchy consolidation in a subpleural location with bronchiectasis noted. Ground-glass opacity with reticular opacities along with ill-defined nodules was also seen.

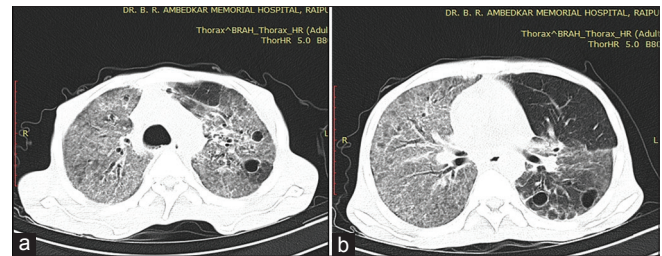


Figure 7: HRCT axial images (a) through the upper lobe (b) subcarinal level showing areas of crazy paving (ground-glass opacity with superimposed interlobular and intralobular septal thickening) and few small cystic lesion. Findings compatible with pneumocystis jiroveci pneumonia

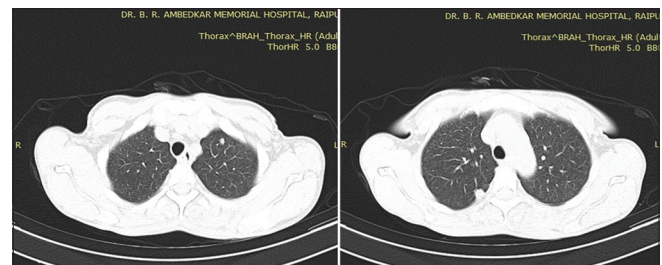


Figure 8: Axial HRCT images through the upper lobes showing subpleural nodules in a case of cryptococcosis

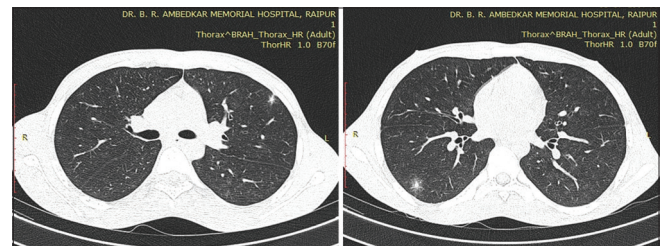


Figure 9: Axial HRCT images showing nodules surrounded by ground-glass opacity (CT-halo sign) in a case of angioinvasive aspergillosis

Table 2: Nodules distribution in TB cases

Distribution of nodules	No. of patients
centrilobular	20
Centrilobular + tree in bud	11
Random + tree in bud	04
Miliary	04

TB: Tuberculosis

Their CD4 counts were 112 and 357 cell/mm³, respectively [Figure 12].

Bacterial pneumonia

One case in our study was diagnosed to be suffering from bacterial pneumonia. HRCT findings include consolidation, bronchiectasis, nodules, and lymphadenopathy [Figure 13].

Magenat *et al.*, and Boisselle *et al.*, reported that focal consolidation was observed in approximately 45–60% of patients with pyogenic infection.^[14,15]

Selwyn *et al.*, found that the combination of focal consolidation of chest radiography and a history of fever for fewer than 7 days was associated with a sensitivity of 48% and a specificity of 94% for the diagnosis of bacterial pneumonia.^[16]

Allen *et al.*, reported that abnormalities may be detected on HRCT in the absence of any CXR findings. These include bronchiectasis and evidence of small airway disease, with

ill-defined centrilobular micronodularity and branching structures or tree-in-bud appearance secondary to mucus impaction in the bronchioles. Mosaic attenuation may also be present due to air trapping.^[7]

Bronchiolitis obliterans

One patient in our study was diagnosed to be suffering from bronchiolitis obliterans. HRCT findings include patchy ground opacities with mosaic attenuation, tubular bronchiectasis diffusely involving bilateral lung fields. Few nodular opacities with a large cystic lesion also noted. His CD4 count was 504 cells/mm³ [Figure 14].

Kaposi sarcoma

One patient in our study was diagnosed to be suffering from Kaposi sarcoma. He presented with complaints

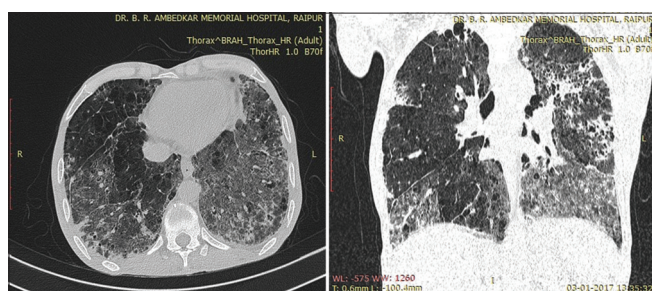


Figure 10: Usual interstitial pneumonia in a 60-year-old male. HRCT axial and coronal reformatted image showing ground-glass opacity with reticular shadowing predominantly involving posterior and lower lung zones. Honeycombing and bronchiectasis can be easily seen

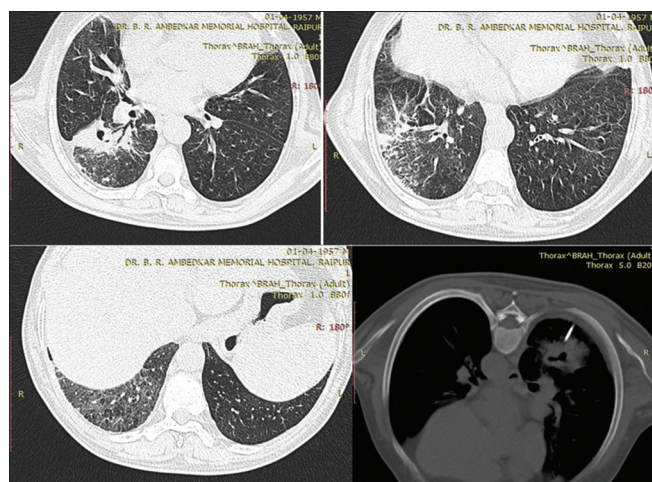


Figure 11: Axial HRCT images through lower lobes showing consolidation and ground-glass opacity with reticular opacities. Few bronchiectatic changes also noted. Last image showing computed tomography-guided biopsy from the lesion. Biopsy demonstrated usual interstitial pneumonia

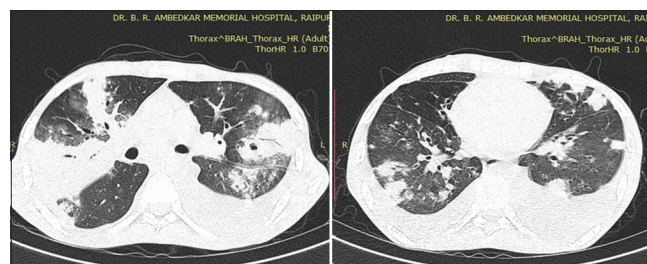


Figure 12: Axial HRCT scan showing the patchy area of airspace consolidation in subpleural in location. Surrounding ground-glass opacity can be clearly seen. Few ill-defined nodules are also noted. Case of bronchiolitis obliterans organizing pneumonia

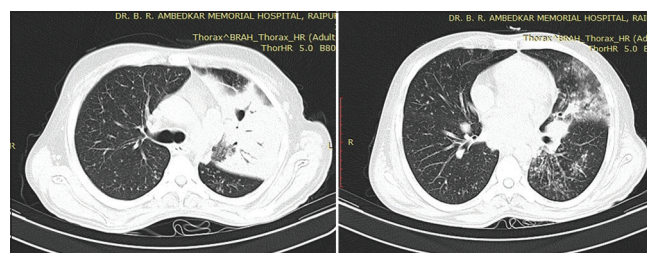


Figure 13: HRCT axial images showing airspace consolidation, focal bronchiectasis, and micronodules in a case of bacterial pneumonia (culture positive for streptococcus)

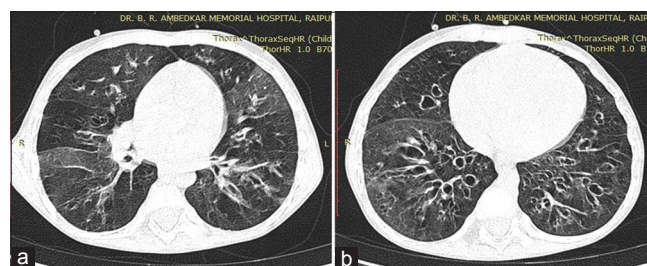


Figure 14: HRCT axial images showing patchy ground-glass opacity with mosaic attenuation (a) and bronchiectatic changes diffusely involving bilateral lower lung likely suggestive of bronchiolitis obliterans (b)

of breathlessness and cough with vascular skin lesions. HRCT findings include peribronchovascular interstitial thickening with flame-shaped nodules in peribronchovascular distribution. Airspace consolidation, ground-glass opacity with reticular opacities and bronchiectatic changes noted involving bilateral lower lobes. Paraseptal emphysema as well as centrilobular emphysematous changes also noted. His CD4 count was 94 cells/mm³ [Figure 15].

Pulmonary thromboembolism

One case in our study was diagnosed to have pulmonary thromboembolism. Thrombus was noted in right main pulmonary artery extending into lobar and segmental branches noted with basal consolidation. Left-sided mild pleural effusion was also seen. His CD4 count was 608 cells/mm³.

Table 3: Diagnostic significance of radiological investigations in diagnosis of pulmonary TB

Radiological diagnosis	Final diagnosis		Total
	Other	Pulmonary TB	
Other			
Count	27	1	28
% within radiological diagnosis	96.4	3.6	100.0
% within final diagnosis	84.4	3.4	45.9
Pulmonary TB			
Count	5	28	33
% within radiological diagnosis	15.2	84.8	100.0
% within final diagnosis	15.6	96.6	54.1
Total			
Count	32	29	61
% within radiological diagnosis	52.5	47.5	100.0
% within final diagnosis	100.0	100.0	100.0

TB: Tuberculosis

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-square	40.123 ^a	1	0.000		
Continuity correction ^b	36.930	1	0.000		
Likelihood ratio	47.716	1	0.000		
Fisher's exact test				0.000	0.000
No. of cases ^b	61				

Parameter	Value (%)	95% Confidence interval (%)
Sensitivity	96.5	80.4–99.8
Specificity	84.3	66.4–94.1
PPV	84.8	67.3–94.3
NPV	96.4	79.7–99.8

PPV: Positive predictive value, NPV: Negative predictive value

The sensitivity and specificity to detect pulmonary TB by HRCT were found to be 96.5% and 84.3%, respectively [Table 3].

We compared the CD4 counts with different outcomes (i.e., death, deterioration, and improvement on follow-up). The mean CD4 count was found to be lower in patients with death, poor treatment responders, and the highest with clinical symptomatic improvement; however, the difference failed to reach statistical significance ($P < 0.0001$) [Figure 16 and Table 4].

Prognostic significance of CD4 count was demonstrated using ROC curves in which 66.9% area comes under the curve with a sensitivity and specificity 72.5% and 62.5%, respectively [Table 5].

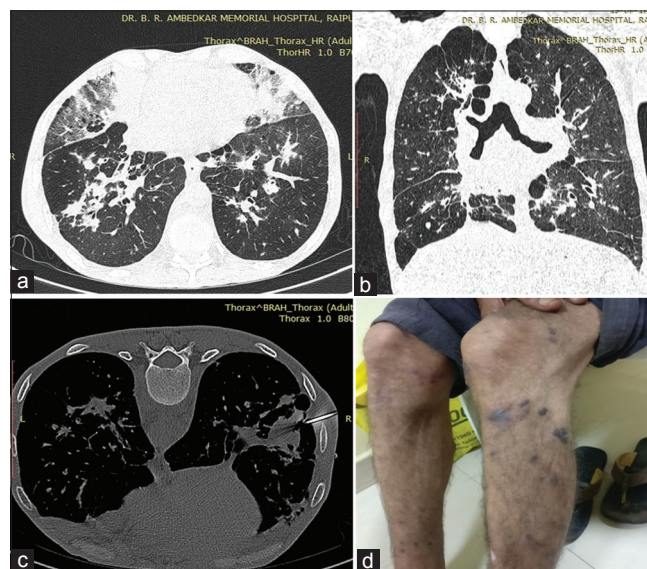


Figure 15: (a) Axial HRCT image and (b) coronal reformatted images showing thickening of peribronchovascular bundles with characteristic flame-shaped nodules in peribronchovascular distribution. Consolidation with ground-glass opacity and reticular opacities noted in the bilateral middle lobe. (c) Image showing computed tomography-guided biopsy from the lesion. Biopsy demonstrated Kaposi sarcoma. (d). Clinical image showing vascular skin lesions.

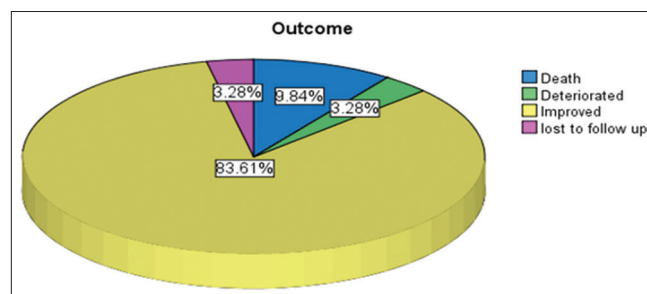


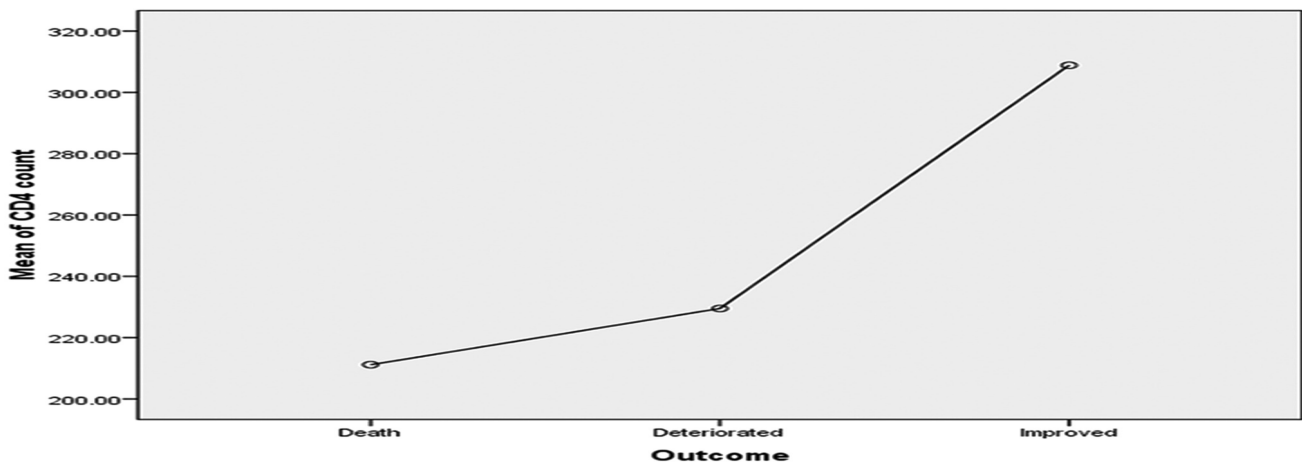
Figure 16: Distribution of outcomes among symptomatic adult HIV-positive patients

Table 4: Comparison of CD4 count in different outcomes in study participants

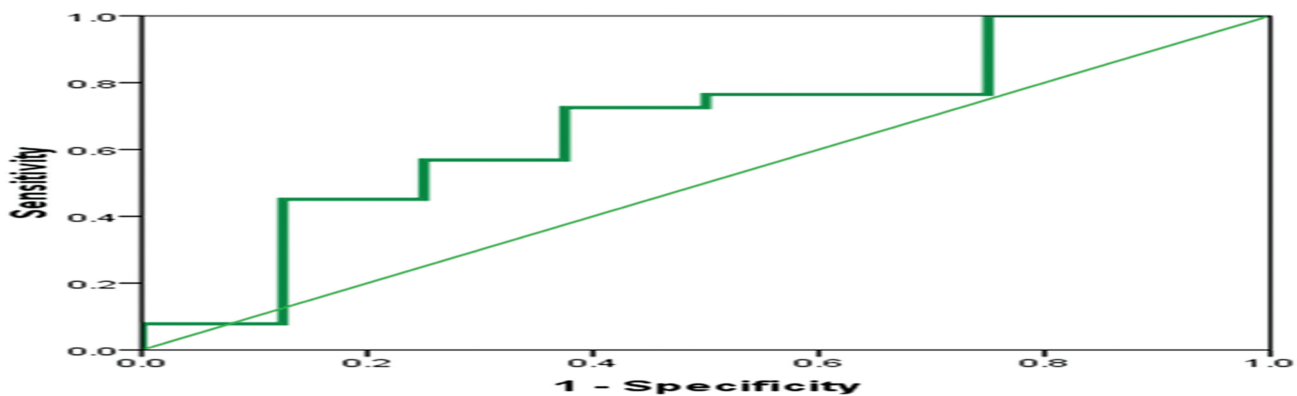
CD4 count	N	Mean	Std. deviation	Std. error	95% Confidence interval for mean		Minimum	Maximum
					Lower bound	Upper bound		
Death	6	2.1117E2	208.54392	85.13770	-7.6868	430.0201	28.00	608.00
Deteriorated	2	2.2950E2	123.74369	87.50000	-882.2929	1341.2929	142.00	317.00
Improved	5	3.0884E2	170.116	23.8211	260.9970	356.689		
	1	2	94	4		3	74.00	710.00
Total	59	2.9622E2	173.21444	22.55060	251.0804	341.3603	28.00	710.00

ANOVA**CD4 count**

	Sum of squares	df	Mean square	F	Sig.
Between-groups	60434.057	2	30217.029	1.007	0.372
Within groups	1679754.078	56	29995.609		
Total	1740188.136	58			

**Table 5: Prognostic significance of CD4 count****Area under the curve**

Test result variable (s):CD4 count			Asymptotic 95% confidence interval		Cutoff	Sensitivity %	Specificity %
Area	Std. Error ^a	Asymptotic Sig. ^b	Lower bound	Upper bound			
0.669	0.108	0.127	0.458	0.880	193	72.5	62.5



CONCLUSION

Pulmonary TB was the most common pulmonary manifestation in HIV patients followed by fungal infection (including PJP and cryptococcosis) and interstitial lung disease (including BOOP and UIP). The incidence of all these disease manifestations fairly correlates with the decline of CD4 counts. Early and proper diagnosis of these pulmonary complications in patients with HIV infection will help clinicians develop a focussed therapeutic approach to patient management.

HRCT is a highly sensitive tool for detecting lung parenchymal and interstitial lesions and allows better characterization of the lesions. Conventional radiography has low sensitivity and specificity and at many times does not lead to a conclusive diagnosis specially in complex situations where multiple infection is commonly seen. The lesions which are not detected or are equivocal on plain radiographs are identified and can be categorized as being active or inactive and thus helps to plan timely management, thereby reducing the morbidity and mortality from respiratory diseases in HIV patients. Hence, we recommend HRCT in the diagnosis, treatment, and follow-up of these patients with pulmonary manifestations. Its noninvasive nature and relatively quicker time of scan make it a suitable choice in these patients.

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Study on Correlation between Endocrine and Metabolic Parameters in Polycystic Ovary syndrome and Thyroid-Stimulating Hormone: Should Normal Thyroid-Stimulating Hormone Level be Redefined?

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Abstract

Introduction: Polycystic ovary syndrome (PCOS) is a fairly common disorder of women in the reproductive age. Thyroid-stimulating hormone (TSH) affects endocrine and metabolic parameters in PCOS are claimed by some researchers.

Purposes: This study was carried out to clarify if there are correlations with endocrine and metabolic parameters in PCOS with TSH.

Methods: A total of 100 PCOS patients of age group between 20 and 35 years and body mass index (BMI) 18.5-30kg/m² were recruited. Forty ($n=40$) healthy female subjects matched for age and BMI were also enrolled as controls. Cases were divided into two groups: Group I (TSH<2.1) and Group II (TSH≥2.1). All variables were again compared between two groups of PCOS cases.

Results: The mean serum BMI, TSH, fasting glucose, fasting insulin, homeostatic model assessment-insulin resistance, total cholesterol, low-density lipoprotein, triglyceride, and very low-density lipoprotein levels were significantly higher in Group II PCOS than Group I PCOS. Moreover, the luteinizing hormone (LH) and LH/follicle-stimulating hormone (FSH) levels were significantly lower in the patients with Group II PCOS than Group I PCOS ($P < 0.05$). Serum FSH, total testosterone, and high-density lipoprotein were unaltered in both groups.

Conclusion: TSH altered endocrine and metabolic parameters in PCOS.

Key words: Polycystic ovary syndrome, Thyroid stimulating hormone, Insulin resistance

INTRODUCTION

Polycystic ovary syndrome (PCOS) is a fairly common disorder of women in the reproductive age. It is characterized by hyperandrogenism and chronic anovulation.^[1,2] It affects 5%–6% of women during the reproductive age group.^[3]

Obesity, insulin resistance (IR), and dyslipidemia, which may predispose patients to metabolic syndrome, are common in PCOS.^[4] Hyperandrogenism usually suggested by the presence of hirsutism (occurs in approximately 80% of PCOS women) and can be documented by measuring androgen levels in the blood. Free testosterone is the most frequently elevated steroid in the blood in PCOS. Circulating levels of total testosterone, androstenedione, and dehydroepiandrosterone are also elevated.^[5] Chronic anovulation may present as irregular menstrual periods or amenorrhea. It is not essential to document anovulation by ultrasonography or progesterone measurements in the presence of a clear clinical history. In fact, PCOS occurs in 85%–90% of women with oligomenorrhea and in

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30%–40% of women with amenorrhea.^[6] Many women with PCOS (between 38% and 88%) have been found to be overweight and obese, and the studies reported that obese PCOS women have more severe hyperandrogenism and related clinical features (such as hirsutism, menstrual abnormalities, and anovulation) than normal weight PCOS women.^[7] It is associated with IR. IR, defined as a metabolic state characterized by a decrease in cellular ability to respond to insulin signaling, appears to be an essential pathophysiologic mechanism in the development of all metabolic complications of PCOS.^[8] It has been suggested by some investigators that IR is present in all PCOS patients.^[9] However, others have reported that IR is not a universal finding, but rather is present in no more than 40%–70% of PCOS patients.^[10]

Hypothyroidism also causes similar problems that are occurred in PCOS like cystic ovaries, ovulatory dysfunction, and anovulation.^[11] Hypothyroidism has been shown to cause many metabolic derangements, such as decrease in glucose disposal or its uptake by muscles or adipose tissues in response to insulin, increase in the level of sex hormone-binding globulin, weight gain, and hyperlipidemia, all of which can lead to IR.^[12,13] In the presence of hypothyroidism, ovarian morphology becomes polycystic. Hence, thyroid disorders are one of the exclusion criteria before making a diagnosis of PCOS in any women. Cystic changes with raised ovarian mass have also been reported in hypothyroidism. Two facts make the picture more interesting, first that both have different etiopathology and second that reportedly thyroid disorders are more common in PCOS subjects.^[12,14]

Recently, in a study by Ganie *et al.* confirmed that the chronic lymphocytic thyroiditis (CLT) girls had higher body mass index (BMI), waist circumference, and systolic blood pressure ($P < 0.001$) than non-CLT age-matched control.^[15] An another study conducted in young women with PCOS concluded that there was no difference in two groups (with or without subclinical hypothyroidism) with respect to BMI, waist circumference or Ferriman–Gallwey score.^[16] Hence, the results were conflicting, but the question is whether normal level of thyroid hormone, particularly thyroid-stimulating hormone (TSH) has any relation with endocrine and metabolic parameters in PCOS.

Therefore, this study was carried out to clarify if there are correlations with endocrine and metabolic parameters in PCOS with TSH.

MATERIALS AND METHODS

Study Design

A community-based case control study was carried out from 2007 to 2011 among women aged 20–35 years

who were permanent residents of West Bengal. PCOS patients with BMI (18.5–30 kg/m²) were recruited from the OPD clinics of the Department of Gynecology in Institute of Postgraduate Medical Education and Research (IPGME&R), Kolkata. This clinical study was approved by the Institutional Ethics Committee (IPGME&R) Kolkata. All of the participants signed informed consent to be included in the study.

Sample Size

Totally 100 PCOS patients between age group between 20 and 35 years were recruited. Healthy age-matched controls ($n=40$) women without PCOS and matched for age BMI were recruited.

Selection of Cases and Control from Sources

Operational definition

Amenorrhea

Amenorrhea was defined as the absence of periods for at least 3 of the previous cycle in patient who had been menstruating previously.

Oligomenorrhea

Oligomenorrhea was considered when length of menstrual cycle was greater than 35 days. It is indirect marker for anovulation in absence of any hormonal evidence.

Normal TSH level – 0.4–4.0 μ /L

Homeostatic model assessment-insulin resistance (HOMA-IR)

Insulin resistance was measured with Homeostatic Model Assessment index (HOMA) = [fasting serum insulin level (μ U/mL) x Fasting plasma glucose (mg/dL)]/405. A value more than two is insulin resistant.

Clinical hyperandrogenism

Hyperandrogenism was defined as presence of hirsutism (modified Ferriman–Gallwey score >5) and or severe acne.

Polycystic ovaries

Polycystic ovaries was defined having ovarian follicles 2–9 mm in diameter and ≥ 12 in number or ovarian volume ≥ 10 cm³ in one or both ovaries on trans-abdominal pelvic ultrasonography (USG). There should be no dominant follicle with size greater than 10 mm in diameter.

Participants selected were undergone three stages of operation.

Stage I: Questionnaire:

Administration of the questionnaire “probable cases” and “probable controls” was identified during the cross-sectional survey.

A “probable case:” A “probable case” was defined as a woman with symptoms suggestive of PCOS (i.e., oligo/amenorrhea/or clinical features of hyperandrogenism) as defined above.

A “probable control”: A “probable control” was defined as a woman with regular menses and no clinical features of PCOS. Probable control group matched for age and BMI of probable PCOS cases were selected. A detailed history of taking drugs was elucidated and all participants who were on oral contraceptive pills, oral hypoglycemic agents and anti-thyroid drugs were excluded from study. They were then selected for Stage 2 examination.

Stage 2: Clinical examination and biochemical investigations

Selected women were examined for the presence of hirsutism, acne, or alopecia. Hirsutism was routinely graded by two physicians independently using the common modified Ferriman–Gallwey (FG) score. If the FG score differed by more than two, reevaluation by a third physician was done and median values were used. Nine areas were examined - upper lip, chin, chest, upper abdomen, lower abdomen, upper back, lower back, thighs, and upper arms. Each area is scored 0–4, resulting maximum score 36. Hirsutism was diagnosed when a score above five was evaluated.

Biochemical Investigations

Venous blood (5 ml) was drawn from both probable cases and probable controls. Blood samples were taken during the 3rd day of the menstrual cycle. Hemolyzed sera were discarded. Serum total testosterone was measured to diagnose biochemical evidence of androgen excess or hyperandrogenemia. Hyperandrogenemia was diagnosed when serum total testosterone level was greater than 55ng/dl Upper normal level of serum total testosterone level was 55ng/dl in our laboratory. Kit was supplied by Radio-pharmaceutical and isotope technology, BARC, Mumbai.

Stage 3: Ultrasound scanning

Pelvic ultrasound scanning on women identified as probable cases and probable controls. Pelvic ultrasound scanning was done on subjects to note the presence of polycystic ovaries.

Inclusion criteria of cases

The diagnostic criteria for PCOS were based on the unified standards formulated by the Rotterdam International Conference in 2003.^[17] Patients with any two of the following three conditions were diagnosed with PCOS: (1) infrequent ovulation or anovulation; (2)

hyperandrogenism or clinical manifestations of high blood androgen; and (3) polycystic ovaries on USG—multiple small follicles (>10–12) and (2–9 mm in diameter) tightly spaced along the periphery of the ovary.

Exclusion criteria of cases such as thyroid dysfunction, hyperprolactinemia, congenital adrenal hyperplasia, androgen secreting tumors, Cushing syndrome, and other diseases were included in the study. Patients were on organizational culture profile (OCP), hypolipidemic, and hypoglycemic drugs and were excluded from the study.

Inclusion criteria of controls

Patients in the control groups exhibited normal menstruation, no clinical or biochemical signs of hyperandrogenism, normal ovaries as defined by ultrasonic examination, and no family history of PCOS and they should be age and BMI matched with cases.

Participants on OCP or conceived were excluded from the study. Chronic kidney disease liver disease cancer patients were also excluded from the study.

A total of 100 PCOS patients between age group between 20 and 35 years were recruited. Healthy age-matched controls ($n=40$) women without PCOS and matched age, BMI recruited.

Other Biochemical Parameters

Blood samples were taken during the 3rd day of the menstrual cycle. Hemolyzed sera were discarded. All assays were completed within 3 days. Serum glucose estimation done by glucose oxidase-peroxidase with kit manufactured by Monozyme India Limited, Secunderabad, insulin by radioimmunoassay with module supplied by Radiopharmaceutical and Isotope Technology, Mumbai. Total serum follicle-stimulating hormone (FSH) and luteinizing hormone (LH) were also measured. Serum TSH, total cholesterol, high-density lipoprotein (HDL), low-density lipoprotein (LDL), very low-density lipoprotein (VLDL), and triglyceride (TG) were also measured.

Statistical Analysis

Statistical analysis was done by descriptive statistics in statistical analysis were carried out using XLSTAT 2018. Descriptive statistics are presented as mean \pm standard deviation for normally-distributed variables. Non-normally distributed variables were compared by the Kolmogorov Smirnov test. Student's *t*-test was used to compare variables with normal distribution and $P < 0.05$ was considered significant. The degree of association between continuous variables was calculated by the Pearson correlation coefficient.

Tables 1: Basic parameters

Basic parameters	Cases=100		Controls <i>n</i> =40	
	Range	Mean	Range	Mean
Age years	20–35	26.42	20–35 years	26.89
BMI kg/m ²	18.5–30	23.49	18.5–30	22.46

BMI: Body mass index

RESULTS

Hormonal and metabolic parameters were screened in the patients with PCOS and in the healthy control subjects.

Basic Parameters [Table 1]

We studied 100 patients with PCOS (mean age 26.42 ± 4.58 years, range 20–35 years; BMI, 23.39 ± 3.22 kg/m²) and 40 years age and BMI-matched healthy controls (mean age 26.89 ± 3.91 years, range 20–35 years; BMI, 22.46 ± 2.6 kg/m²).

Difference between mean age and BMI of 75 obese PCOS cases and mean age obese controls is not statistically significant.

Comparing Parameters between in Women with PCOS and Controls

The mean serum TSH, LH, LH/FSH, fasting insulin, HOMA-IR, total testosterone, TG, and VLDL levels were significantly higher, and the HDL levels were significantly lower in the patients with PCOS than controls ($P < 0.05$). Serum FSH and glucose were total cholesterol unaltered in both groups [Table 2].

Determination of Cutoff Value of TSH

TSH is positively correlated with HOMA-IR ($r=0.525$, $P<0.0001$). The correlation between TSH and IR was shown in Figure 1.

The association between TSH and IR, evaluated using the ROC curve, showed a cutoff value for TSH of 2.1 mIU/L. At this value, sensitivity of 80.9% and specificity of 61.8% for diagnosis of IR using HOMA-IR (value above 2 is insulin resistant) [Figure 2].

Based on cutoff value, PCOS cases were divided into two groups: Group I (TSH < 2.1) and Group II (TSH \geq 2.1). All variable were again compared between two groups of PCOS case as shown in Table 3.

All Variable between Two Groups of PCOS Cases

The mean serum BMI, TSH, fasting glucose, fasting insulin, HOMA-IR, total cholesterol, LDL, TG, and VLDL levels were significantly higher in Group II PCOS than Group I PCOS. Moreover, the LH and LH/FSH levels were significantly lower in the patients with Group II PCOS than Group I PCOS ($P < 0.05$). Serum FSH, total testosterone, and HDL were unaltered in both groups.

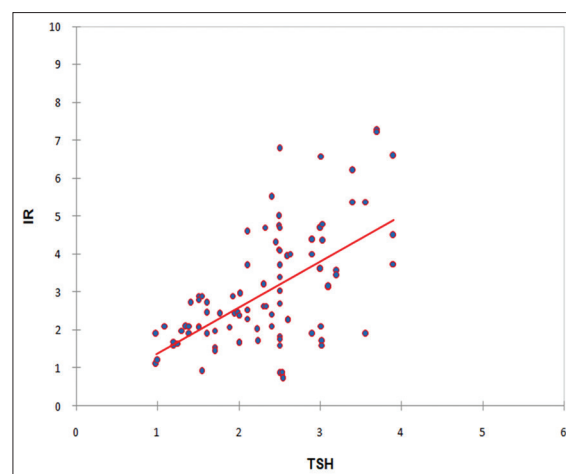


Figure 1: The correlation between thyroid-stimulating hormone and insulin resistance (IR) (homeostatic model assessment IR)

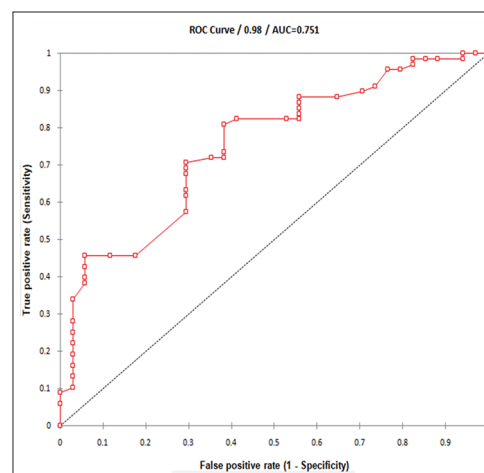


Figure 2: Receiver operating characteristic curve to evaluate the association between thyroid-stimulating hormone and IR

The Correlations between Biochemical and Hormonal Parameters with TSH

These were shown in Table 4.

A significant positive correlation was found between the TSH with glucose ($r=0.235$, $P=0.017$), insulin ($r=0.492$, $P=0.001$), HOMA-IR ($r=0.525$, $P<0.001$), testosterone ($r=0.298$, $P=0.02$), cholesterol ($r=0.232$, $P=0.019$), LDL ($r=0.199$, $P=0.045$), TG ($r=0.310$, $P=0.002$), and VLDL ($r=0.305$, $P=0.02$). Negative correlation was found between TSH with LH/FSH ($r=-0.249$, $P=0.012$) and LH ($r=-0.363$, $P=0.01$). However, no correlation were found between TSH with FSH ($r=0.28$, $P=0.00$) and HDL ($r=0.106$, $P=0.289$).

DISCUSSION

This study showed that TSH levels >2.1 mIU/L being associated with IR and other hormonal and metabolic variables evaluated were also altered at that

Table 2: Comparing parameters between women with PCOS cases and controls

Parameters	PCOS cases n=100	PCOS controls n=40	P value	Significant or not
Age	26.43±4.58	26.89±3.92	0.491	Not significant
BMI kg/m ²	23.49±3.228	22.46±2.6	0.078	Not significant
TSH	2.37±0.708	1.6±0.65	0.001	Significant
LH, µ/ml	11.73± 5.99	8.61±3.86	0.002	Significant
FSH, µ/ml	4.42±1.622	4.56±1.99	0.621	Not significant
LH/FSH	2.2±0.76	0.92±0.287	<0.001	Significant
Glucose mg/dl	87.24±9.51	88.98±11.04	0.353	Not significant
Insulin µ/ml	15.02±7.28	8.97±5.3	0.001	Significant
HOMA-IR	3.7±1.49	1.98±1.3	<0.001	Significant
Total testosterone ng/dl	85.99±41.31	8.91±5.41	0.0001	significant
Cholesterol mg/dl	175.79±17.77	170.64±21.89	0.972	Not significant
LDL mg/dl	105.23±16.26	104.71±21.38	0.88	Not significant
HDL mg/dl	42.4±4.65	47.43±4.5	0.0001	Significant
TG mg/dl	134.66±43.15	117.36±28.32	0.022	Significant
VLDL mg/dl	27.31±8.9	23.48±5.17	0.01	Significant

n: Number. BMI: Body mass index, HDL: High-density lipoprotein, LDL: Low-density lipoprotein, VLDL: Very low-density lipoprotein, TG: Triglyceride, HOMA-IR: Homeostatic model assessment-insulin resistance, LH: Luteinizing hormone, FSH: Follicle-stimulating hormone, TSH: Thyroid-stimulating hormone, PCOS: Polycystic ovary syndrome

Table 3. Variable compared between two groups of PCOS cases

Parameters	PCOS Group I n=32	PCOS Group II n=68	P value	Significant or not
Age	25±5.47	26±3.98	0.063	Not significant
BMI kg/m ²	21.99±2.44	28.68±4.69	<0.001	Significant
TSH	1.65±0.34	2.82±0.466	0.001	Significant
LH, µ/ml	7.22±3.76	12.53±4.87	0.002	Significant
FSH, µ/ml	4.6±1.778	4.28±1.52	0.33	Not significant
LH/FSH	1.99±0.	542.59±0.9	<0.001	Significant
Glucose mg/dl	83.92±7.1	89.17±10.26	0.007	Significant
Insulin µ/ml	12.86±4.42	16.6±8.25	0.012	Significant
HOMA-IR	2.64±1.01	3.58±1.65	0.02	Significant
Testosterone ng/dl	77.56±31.99	81.8±45.36	0.228	Not significant
Cholesterol mg/dl	164.66±22.97	183.29±19.67	<0.001	Significant
LDL mg/dl	97.68±14.5	110.404±15.4	<0.001	Significant
HDL mg/dl	43.29±5.26	41.9±4.24	0.153	Not significant
TG mg/dl	116.58±40.74	146.94±40.9	0.001	Significant
VLDL mg/dl	23.31±8.15	29.57±8.6	0.001	Significant

BMI: Body mass index, HDL: High-density lipoprotein, LDL: Low-density lipoprotein, VLDL: Very low-density lipoprotein, TG: Triglyceride, HOMA-IR: Homeostatic model assessment-insulin resistance, LH: Luteinizing hormone, FSH: Follicle-stimulating hormone, TSH: Thyroid-stimulating hormone, PCOS: Polycystic ovary syndrome

Table 4: Correlations between biochemical and hormonal parameters with TSH

Parameters	PCOS cases n=100 r value	P value
BMI	0.419	<0.0001
LH/FSH	-0.249	0.012
LH	-0.363	0.01
FSH	0.28	0.00
Glucose	0.235	0.017
Insulin	0.492	0.001
HOMA-IR	0.525	<0.001
Testosterone	0.298	0.02
Cholesterol	0.232	0.019
LDL	0.199	0.045
HDL	0.106	0.289
TG	0.310	0.002
VLDL	0.305	0.02

BMI: Body mass index, HDL: High-density lipoprotein, LDL: Low-density lipoprotein, VLDL: Very low-density lipoprotein, TG: Triglyceride, HOMA-IR: Homeostatic model assessment-insulin resistance, LH: Luteinizing hormone, FSH: Follicle-stimulating hormone, TSH: Thyroid-stimulating hormone, PCOS: Polycystic ovary syndrome

defined cutoff value. In our study, we found following abnormalities.

Abnormalities Related to Glucose Concentration and Insulin Resistant

We found a linear correlation between TSH and fasting glucose concentrations and there was difference between two groups of PCOS but no differences between PCOS cases and controls. A study in India did not find any relation with serum TSH and glycemia.^[18] Mueller *et al.* found that in women with PCOS, TSH ≥ 2.0 µIU/mL is associated with IR independently of BMI and age, and hypothyroid disturbances and elevated TSH levels are common findings among women with PCOS.^[19] PCOS women show a high prevalence of metabolic disturbances including IR, dyslipidemia, and chronic low-grade inflammation.^[20]

These findings bring to mind the question that does the hypothyroidism intensity have additional impact over IR? And is this IR in fact due to changes in thyroid hormones.

Abnormalities Related to Lipid Profile

In our study, we concluded gross alteration in all lipid parameters except HDL between two groups of PCOS cases. No alteration in HDL between two groups of PCOS and we could not explained it. Conflicting results were there on relationship among lipid parameters and SCH. Tuzca *et al.* concluded higher LDL in the SCH with PCOS and no changes in TG and HDL when compared with controls.^[2,3] Ganie *et al.* concluded high triglyceride in the SCH group with PCOS with the control group^[18,21,22] comparing to the control group.^[23,24] Some studies claimed that no alteration in lipid levels in patients with PCOS and SCH compared to euthyroid case. Larger multi-centric studies are needed.

Gonadotropin Abnormalities

In our study, LH is lower in Group II PCOS (TSH ≥ 2.1) than Group I PCOS. No data were available on this finding. It might be due to effect of BMI.

A possibility arises that some obesity-associated factor may suppress GnRH pulse amplitude or pituitary LH responsiveness. Leptin acting at the level of the pituitary or hypothalamus may dampen LH secretion in obese PCOS individuals. Some authors have proposed this hypothesis, like La Zovic *et al.* noticed that there is significant positive correlation between LH and serum leptin level in non-obese PCOS negative correlation between these serum LH and leptin in obese PCOS cases.^[25] We can assume this study that leptin modulates hypothalamic-pituitary-gonadal axis, and attenuation of serum LH obese PCOS is due to leptin resistance state. A second possibility is decreased LH secretion in obese PCOS is due to beta-endorphin.^[26]

CONCLUSION

- TSH altered endocrine and metabolic parameters in PCOS
- This study showed that TSH levels >2.1 mIU/L being associated with IR and other hormonal and metabolic variables evaluated were also altered at that defined cutoff value.
- Our study also offers the possibility that the potential use of TSH as a predictor that can be involved in PCOS-related metabolic disturbances.

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Study of Bacteriological and Clinical Profile of Community Acquired Pneumonia in Type 2 Diabetes Patients in Tertiary Care Hospital, Warangal

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Abstract

Aim: In this study we proposed to determine whether the clinical or radiological findings, the causative organisms or the outcome of pneumonia are modified by presence of diabetes mellitus as underlying disease.

Introduction: Infections of respiratory tract are perhaps the most common human ailments. They are the source of discomfort, disability and loss of many work days for most adults. They lead to substantial morbidity and mortality in young children and elderly.

Materials And Methods: The study was conducted for a period of 1 year, from July 2016 to July 2017. A detailed history was taken in all the patients with respect to presenting complaints predisposing factors and accompanying illness.

Results: Study conducted in a group of 60 people of which 30 were diabetics and 30 non diabetics with maximum people between 40-75yrs.

Conclusions: In patients with pneumonia, Diabetes mellitus is a significant prognostic factor of mortality. Comorbidities of the patients rather than microbiological findings attribute to adverse outcome.

Key words: Blood sugar, Diabetes mellitus, Pneumonia

INTRODUCTION

Infections of respiratory tract are perhaps the most common human ailments. They are the source of discomfort, disability and loss of many work days for most adults. They lead to substantial morbidity and mortality in young children and elderly. Among the respiratory infections, pneumonia is a common cause of hospital admission, although a majority are treated in out-patient settings. Pneumonia presents as a challenge to physicians, have to decide on therapy without the benefit of definitive etiological diagnosis as the clinical features of pneumonia are neither sensitive nor reliable guide in permitting an etiological diagnosis.

Underlying diseases (COPD, compromised immune system, dementia, GERD, etc.) increase susceptibility of the patients for pneumonia; therefore it is not surprising that epidemiological studies have found one or more of these conditions in a high proportion of such episodes.^{1,2} Alternatively habitual pathogens could show particular patterns of antimicrobial resistance.³ Undoubtedly the knowledge of these microbiological characteristics is critical and represents the basis for empirical treatments. Serious co-existing illness have been identified as modifying factors of severity of pneumonia.^{1,4} On the basis of these appreciation,¹ published guidelines on pneumonia advocate specific criteria for antibiotic selection and the management of patients in the presence of co-morbid diseases.⁵ Diabetes mellitus is a very prevalent chronic metabolic disorder that is present in about 5-10% of elderly population. Several aspects of immunity such as polymorphonuclear leukocyte function i.e. leukocyte adherence, chemotaxis, phagocytosis and bacterial activity of serum are depressed in patients with diabetes.^{6,7} For patients with pneumonia, diabetes mellitus is also one of the most common underlying diseases.^{1,2,8}

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In this study we proposed to determine whether the clinical or radiological findings, the causative organisms or the outcome of pneumonia are modified by presence of diabetes mellitus as underlying disease.

Aims and Objectives

To compare pneumonia in diabetics and non-diabetics in the following aspects Clinical presentation of pneumonia, Bacteriological etiology of pneumonia, Complications and prognosis, Radiological patterns.

MATERIALS AND METHODS

30 diabetic patients and 30 non-diabetic patients with bacterial pneumonia admitted in Mahatma Gandhi Memorial Hospital, Warangal. The study was conducted for a period of 1 year, from July 2016 to July 2017. A detailed history was taken in all the patients with respect to presenting complaints (like fever, new or increasing sputum production, dyspnoea and chest pain) predisposing factors and accompanying illness.

A diagnosis of diabetes mellitus was based on previous clinical and/or biochemical diagnosis and/or treatment with oral anti-diabetic agents or insulin. Alternatively, diagnosis could be established during this episode of pneumonia when the fasting plasma glucose concentration was ≥ 126 mg/dl and/or after ingestion it was ≥ 200 mg/dl on two or more separate occasions. A thorough clinical examination was carried out as per proforma.

Laboratory investigation like haemoglobin, total count, differential count, erythrocyte sedimentation rate, blood urea, creatinine, random blood sugars, fasting blood sugars, post prandial blood sugars were done. The investigations were repeated as and when necessary.

In all the patients, chest x-ray PA view was taken on admission and 7 days after antibiotic therapy. In few patients chest x-ray lateral view was also taken. Ultrasound chest was also done in few cases.

Sputum was collected for bacteriological examination after rinsing the mouth with saline before institution of antibiotic therapy and subjected to following tests.

Macroscopic examination: Sputum was examined macroscopically with respect to quantity, colour, odour and evidence of haemoptysis.

Sputum microscopy: All the sputum smears were stained with gram's stain. Those smears which showed more than 25 polymorphs per low power field and less than 10 squamous epithelial cells per low power field was considered as appropriate sample 2 and others as inappropriate. Sputum was also examined for AFB by Ziehl neelson (ZN) stain.

Sputum culture: The purulent portion of the sputum was inoculated on blood agar, MacConkey's medium and heat blood agar. These were read after overnight incubation.

Inclusion Criteria

Type 2 diabetic patients and non-diabetic patients who fulfill all the following criteria Fever, productive or non productive cough with or without chest pain or breathlessness. X-ray chest PA view showing homogenous or non homogenous opacities. Sputum gram staining and culture showing pathological organisms.

Exclusion Criteria

Features suggestive of viral and fungal pneumonia and culture showing fungal growth. Patients diagnosed to have tuberculosis. Patients who are HIV positive or with other immunocompromised states. Patients with upper respiratory tract infections.

RESULTS

Table 1: Comparison of age in years between two groups

Age in years	Non-diabetic		Diabetic	
	Number	Percent	Number	Percent
21-30	3	10	1	3.3
31-40	6	20	5	16.7
41-50	11	36.7	13	43.3
51-60	10	33.3	11	36.7
Total	30	100	30	100
Mean \pm SD	44.3 \pm 9.37		46.43 \pm 8.65	

Samples are age matched with $P=0.3641$. The average age in SG was 46.43 ± 8.65 yrs and in CG were 44.3 ± 9.37 yrs. Most of the patients (80% in SG and 70% in CG) were between 40 to 60 years.

Table 2: Comparison of sex between two groups

Sex	Non-diabetic		Diabetic	
	Number	Percent	Number	Percent
Male	20	66.7	24	80
Female	10	33.3	6	20
Total	30	100	30	100

Samples are age matched with $P<0.250$. Most of the patients in both groups were males (66.7% in CG and 80% in SG). There was no statistically significant difference regarding sex in both the groups.

Table 3: Comparison of concomitant underlying illness between two groups

Concomitant underlying illness	Nondiabetic		Diabetic	
	Number	%	Number	%
Asthma	1	3.3	2	6.7
COPD	5	16.7	7	23.3
IHD	3	10	6	20

The commonly associated co morbidities in CG and SG were Asthma (3.3% vs 6.7%), COPD (16.7% vs 23.3%) and IHD (10% vs 20%). There was no statistically significant difference of associated co morbidities in between two groups ($p=0.207$).

Table 4: Comparison of habits between two groups

Habits	Nondiabetic		Diabetic		P value
	Number	%	Number	%	
Smoking	6	20	9	30	0.371
Alcohol	2	6.7	4	13.3	0.389

There was no statistically significant difference of habits (smoking and alcohol) between two groups.

Table 5: Comparison of RR, SBP, DBP and SPO2 between two groups (results are presented in Mean±SD)

Parameters	Non-diabetic	Diabetic	P value
RR (bpm)	24.7±3.27	26.43±2.96	0.035
SBP (mmofHg)	124.1±18.04	112.56±20.11	0.022
DBP (mmof Hg)	81.83±9.85	78.2±9.84	0.158
SPO2 (%)	86.96±6.17	84.76±7.03	0.202
(25,75 percentile)			

There was statistically significant difference in the vital signs (RR, SBP) between two groups.

Table 6: Comparison of chest X-ray findings

Chest X-ray findings	Non-diabetic		Diabetic	
	Number	%	Number	%
Unilobe	21	70	12	40
Multi lobe	9	30	18	60
Total	30	100	30	100
Inference	P=0.019*			

Multi lobe involvement is more in Diabetic group (60%) than in Non-diabetic group and the difference is found to be statistically significant

DISCUSSION

In the present study I have compared following parameters like age, sex, clinical features, concomitant underlying diseases, vital data, investigations, complications and PSI class between diabetic and non diabetic patients with pneumonia

Age

Present study		Miquel et al.		Pradeep.et.al	
SG	CG	SG	CG	SG	CG
46.43±8.65	44.3±9.37	62yrs	54yrs	57.93±9.71yrs	56.90±11.83yrs
yrs	yrs				

Pradeep *et al.* reported that diabetic patients with pneumonia were significantly older than 57yrs.in a study conducted in a group of 60 people of which 30 were diabetics and 30 non diabetics.with maximum people between 40-75yrs.

Miquel *et al.* also observed that most patients were older than 62yrs.in a study conducted on 106 diabetic patients with pneumonia and 554 non diabetic patients with pneumonia

Akbar DH has also reported a higher age incidence.

In the present study average age of presentation was 46yrs with maximum people between 40-60yrs(80%).

Sex

Sex	Present study	Miquel et al.	Pradeep et al.
Male	80%	60%	66.7%
female	20%	40%	33.3%

Miquel *et al.*reported that patients were predominantly males. Pradeep *et al.*also reported male predominance.⁵⁰ In the present study also males were predominant.

Concomitant Underlying Illness

Present study	Miquel et al.	Pradeep et al.
25%	56%	27%

Miquel *et al.*reported that 56%of the patients with diabetes had concomitant underlying disease along with diabetes. Pradeep *et al.*showed that 27% of patients had concomitant underlying disease. Present study had 25% of patients with concomitant disease in the form of COPD, asthma and CVA.

Organisms

Miquel *et al.*, Pradeep *et al.*have reported that there was no significant difference in microbiological results in patients with diabetes and non diabetes.

The present study also showed no statistically significant difference in microbiological results in two groups.

Spomenka *et al.*reported that staph aureus and gram negative organisms such as klebsiella, E. coli, enterobacter, pseudomonas and acinetobacter are common organisms in diabetes.

Palmar DL reported that gram positive cocci such as strep pneumoniae are responsible for majority of infections in diabetic patients followed by agents such as H influenza.

The present study has shown that common organisms are strep pneumonia (30%) pseudomonas (16%) and polymicrobial (16%).

Complications

Koziel H *et al.*reported that the most common complications of pneumonia in diabetics were pleural effusion,empyema and bacteremia. Miquel *et al.*reported that pleural effusion was significantly more in diabetic patients and there was difference between other risk factors.

Sayali bhambar *et al.* in a study conducted in pneumonia patients of which 50 were diabetics and 50 were non diabetics observed pleural effusion (6% vs 6%) and septic shock (20% vs 14%).

In the present study patients had complications in the form of septic shock (16%), pleural effusion (13%), renal failure (3%) and MODS (3%) which was more compared to non diabetics.

Chest X-Ray

Multilobe involvement in diabetics

Present study	Pratik <i>et al.</i> study
60%	64%

In a study by Pratik ranjan *et al.* in Kolhapur, D.Y. Patil medical college conducted on 50 CAP patients of which 25 were diabetic and 25 non-diabetic, it was observed that 64% of diabetics had multilobar involvement. Saibal *et al.* showed that on comparison of chest X-Ray, unilateral lobe infiltration was more in non-diabetic patients.

In the present study patients showed statistically significant multilobar involvement in diabetics.

PSI - Class

Miquel *et al.* reported that majority of non diabetics presented with PSI class 1 in comparison with diabetics who in majority presented with class 4 which was statistically significant.

Pradeep *et al.* reported that majority of non diabetics presented with PSI class 1 in comparison with diabetics who in majority presented with class 4 and 5 which was statistically significant.

In the present study, majority of diabetics presented in class 4 and 5 which was significant. Diabetes mellitus has been associated with many alterations of the immune system. In a review of the subject by Joshi *et al.*, the most significant changes were identified within humoral-mediated immunity, particularly related to the polymorphonuclear function.

CONCLUSION

In patients with pneumonia, Diabetes mellitus is a significant prognostic factor of mortality.

Polymicrobial etiology, multilobe involvement and increased severity in the form of high PSI score are associated with poor prognosis.

Comorbidities of the patients rather than microbiological findings attribute to adverse outcome.

Associated comorbidities like CVA, IHD, COPD and asthma had poor outcome in both the groups. However, diabetics had worse outcome compared to non diabetics. Thus emphasizing on the fact that more efforts are needed to increase awareness of impact of uncontrolled DM on the clinical outcome of CAP.

The clinical and bacteriological study of 30 cases of pneumonia in diabetics and 30 cases of pneumonia in non diabetics conducted in Mahatma Gandhi Memorial Hospital, attached to Kakatiya Medical College, Warangal during a period from July 2016 to July 2017. Cases were selected randomly and enrolled for study, literature on etiopathogenesis, bacterial flora, clinical features, investigations and management of pneumonia in diabetics and non diabetics were reviewed.

Results were analysed and compared between diabetic and non diabetic group with reference to age, sex, underlying concomitant disease, clinical features, complications, organisms, PSI scoring. Clinical data was compared with the observation of various workers. The important observation made during this study are summarized as follows:

Males are affected more than females in both the groups, although it was statistically not significant. The average age group of patients in diabetics was 46 yrs in comparison with non diabetics which was 44. Most of the patients were in the age group of 40-60 yrs. The concomitant underlying illness were COPD, IHD, asthma and CVA in both the groups there was no statistically significant difference of associated comorbidities in both groups. There was no statistically significant difference in habits like smoking and alcoholism. In comparison between two groups. On chest X-ray multilobe involvement was significantly more in diabetics (60%) than in non diabetics (30%). On sputum gram staining, GPC were significantly more detected in non diabetic (36.7%) when compared to diabetics. Although there was no statistically significant difference. Polymicrobial organisms were at a higher rate in diabetics compared to non diabetics. Complications were more common in diabetic group, like pleural effusion, septic shock, renal failure and MODS. Majority of non diabetics presented under PSI class 1 when compared to diabetics where majority of them were under PSI class 3 and 4. No statistically significant difference was found in sex distribution in two groups.

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Study of Haematological Manifestations, among Alcoholics in Tertiary Care Hospital

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Abstract

Introduction: Alcohol consumption is known for morbidity and mortality, being a serious health hazard of the people in the world. Multiple organs can be involved like Hepatobiliary system, cardiovascular system, Central nervous system, Hemopoietic system. Alcohol can lead to all types of anemia with suppression of bone marrow.

Materials and Methods: Hematological parameters of 49 adult patients who are moderate alcoholics, 26 patients were severe alcoholics and who were admitted in MGM Hospital, Kakatiya Medical College, Warangal, were included in the study.

Results: Among these 75 patients 60% (45) of the alcoholics had anemia. The mean hemoglobin was 9.2gms% among moderate alcoholics and 9.0gm% among severe alcoholics.

Conclusions: Alcoholism was more common among men in middle aged group and a feature of lower socio economic group. Anemia was a predominant feature among chronic alcoholics. All types of anemia were seen in alcoholics. Microcytic hypochromic anemia, macrocytic anemia, normochromic normocytic anemia.,

Key words: Alcohol, Hematological manifestations, Megaloblastic

INTRODUCTION

Alcoholism represents one of the most serious worldwide socio-economic health problem. An alcoholic is a person who consumes an amount of alcohol capable of producing pathological changes. The amount of alcohol capable of producing diseases, depend on variety of factors including genetic predisposition malnutrition and concomitant viral infection of the liver. According to national council of alcoholism and drug dependence alcoholism is a primary chronic disease with a genetic psychosocial and environmental factors influencing its developmental manifestations. It is characterized by continuous or periodic impaired control over drinking over pre occupation with the drug alcohol and distortion in thinking most notably denial. According to the

National Council of Alcoholics, adults who drank in past year 64%¹.

Mortality

As per National Council of Alcoholism number of alcohol induced death excluding accidents and homicides 21,081.1 No. of alcoholic liver disease deaths 12,5481 The office for national statistic revealed that number of deaths due to alcohol was 4144 in 1991 have increased to 8386 by 2006¹. Hence alcohol consumption is known for morbidity and mortality, being a serious health hazard of the people all over the world. Multiple organs can be involved like Hepatobiliary system, cardiovascular system, Central nervous system, Hemopoietic system. Many times the hematological changes are left undetected and untreated which could progress to cardiac failure. Early detection and treatment of hematological changes can prevent complications and reduce the mortality; these are the basis and the need for the study.

Aims and Objectives

To describe hematological changes in alcoholics. To study the hematological changes with respect to the quantity of alcohol consumption and duration of alcohol

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consumption. To compare the hematological changes occurring in moderate and severe alcoholics.

MATERIALS AND METHODS

Source of Data: Patients who were admitted in MGM Hospital, Kakatiya Medical College, Warangal, Telangana state.

Method of Collection Data

Samples Size: 49 adult patients who are moderate alcoholics, 26 patients who are severe alcoholics and 67 Male patients and 8 female patients.

Inclusion Criteria

All patients who are moderate alcoholics that is who consume alcohol less than 80 to 90 mg proof alcohol that is about 11 drinks per day or 80 mg of proof alcohol three or four times a week.

All patients who are severe alcoholics that is who consume more than 80 to 90 mg proof alcohol daily or more than 11 drinks per day Patients attending and admitted Mahathma Gandhi Memorial Hospital Warangal attached to Kakatiya Medical College, Warangal.

Exclusion Criteria

All patients who are less than 18 years, Patients with other hepatic disorders and Patients receiving hepatotoxic drugs.

RESULTS AND ANALYSIS

The Table 1 shows the maximum (68%) alcoholics are from 31 years to 50 years age group.

The Table 2 shows the maximum 89.4% alcoholics were males and 11.6% are females.

The Table 3 shows the maximum alcoholics 72% (54/75) belongs low socio economic status group.

The Table 4 shows the major complaint are 60% (45/75) from alcoholics, in addition jaundice 40%, pedal edema 28%, pain abdomen 25%, hematemesis 20%, breathlessness 21%, altered sensorium 21% and 10.6% melena.

The Table 5 shows that maximum 62.6% of alcoholics are above 10 years duration and below 20 years.

The Table 6 shows that 60% of alcoholics are presenting with pallor, in addition icterus 40%, pedal edema 28% and parotid swelling 24% clubbing 20%.

Table 1: Distribution of age in years

Age	Alcoholic	
	No.	%
21-30	13	17.4
31-40	24	32.00
41-50	27	36.00
51-60	11	14.6
Total	75	100.00
Mean±SD	45.34±11.20	

Table 2: Gender frequency distribution among study population

Gender	Alcoholic	
	No	%
Male	67	89.4
Female	8	11.6
Total	75	100

Table 3: Frequency distribution of socio-economic status among the study group

SES	Frequency	Percentages
LowSES	54	72.00
Middle SES	21	28.00
Grand Total	75	100.00

Table 4: Distribution of presenting complaints among the study group

Chief complaints	Alcoholic (n=75)	
	No	%
Jaundice	30	40.0
Pain Abdomen	19	25.33
Dist Abdomen	45	60.00
BilatPedEdma	21	28.00
Hematemesis	15	20.00
Malena	8	10.67
Altered Sensorium	16	21.33
Breathlessness	16	21.33

Table 5: Duration of alcohol consumption in years among the study group

Duration in years	Number	%
1-10 Years	19	25.33
11-20 Years	47	62.66
>20 Years	9	12.00
Total	75	100

1. The Table 7 shows the maximum (73.3%) alcoholics are presenting with abnormal abdominal findings.
2. Among them 53% hepatomegaly, 13% ascitis and 6% Splenomegaly.

The Table 8 shows 20% of alcoholics presenting with altered sensorium than pre-coma (6.6%).

Comparison of Complete Blood Count In Moderate And Severe Alcoholics

Haemoglobin slight reduction in both moderate and severe alcoholic. Mean WBC total count is elevated. Mean RBC count is markedly reduced. $P < 0.0002$ * S. The Mean Corpuscular Value elevated in severe alcoholics as compare with moderate alcoholics. The Mean Corpuscular haemoglobin reduced in severe alcoholics as compare with moderate alcoholics. The Mean Corpuscular haemoglobin Concentration reduced in severe alcoholics as compare with moderate alcoholics. $P < 0.00004$ * S. The Packed cell volume elevated in severe alcoholics as compare with moderate alcoholics. The platelet count reduced in severe alcoholics as compare with moderate alcoholics. $P < 0.002$ * S

Peripheral Blood Smear of Alcoholic in study group.

- The microcytic hypochromic anemia picture is more (28%) as compared with Macrocytic anemia presenting picture is 26% in study group
 - Dimorphic anemia 8.88%.
 - Thrombocytopenia 10.6%
 - Pancytopenia 4%.
- The Erythroid hyperplasia Among the moderate alcoholics 6.6% and 2.6 in severe alcoholics
 - Megaloblastic anaemia presents 13.2% in severe alcoholics as compared 4% in moderate alcoholics.

Table 6: Findings on physical examination in alcoholic study group

On Examination	Number (n=75)	Percentage
Pallor	45	60.0
Icterus	30	40.0
Clubbing	15	20.0
Pedal -edema	21	28.0
Parotid-Swelling	18	24.0
Other	19	25.33

Table 7: Per abdomen findings among study alcoholic group

P/A findings	Number (n=75)	%
Abnormal	55	73.33
Hepatomegaly	40	53.33
Splenomegaly	5	6.66
Ascitis	10	13.33

Table 8: CNS manifestations

CNSAbnormal	Number (n=75)	%
Pre Coma	5	6.66
AlteredSensorium	15	20.00

- Myeloidysplasia picture, 5.3% in severe alcoholics and 4% in moderate alcoholics.
- Sideroblastic picture more (6.6%) in severe alcoholics and 1.3% in moderate alcoholics.
- Vacuolated RBC are seen 5.3% in moderate alcoholics and 4% in severe alcoholics.

Comparison of LFT parameters in Moderate and Severe Alcoholic

- The table shows abnormal LFT 30/75 (40%). The total bilirubin raised in both moderate and severe alcoholics. $P < 0.000$.
- Direct bilirubin raised more in severe alcoholics as compared with moderate alcoholics. $P < 0.003$.
- The proteins levels are very low in severe alcoholics and albumin levels are very low, as compared with moderate alcoholics.
- SGOT & SGPT is more elevated in severe alcoholics.
- ALP is significantly raised in severe alcoholics. $P < 0.0006$ *S

DISCUSSION

The Present Study was Undertaken

- To describe haematological changes in alcoholics.
- To study the haematological changes with respect to the quantity of alcohol consumption and duration.
- To compare the haematological changes in moderate and severe alcoholics

Demographic Details

In our present study 75 alcoholic patients and their age group ranged from 20 years to 60 years, mean age being 45.34. In a similar study done by T. Oduola *et al.*¹ in Nigeria out of 200 patients age of patients ranged from 20 years to 57 years mean age being 36.04 ± 11.28 years.

In our study the maximum prevalence's of alcoholics were in the age group 31-50 years (51/75) 68%. There was less prevalence of alcoholism below 20years and above 60 years. This could be probably because middle age group people belonging to lower socioeconomic status are hard working and after hard stress and want to relax in the evening by taking alcohol. The maximum number of hematological abnormalities ie anemia was seen in age group of 31 to 60 years.

In a similar study done by D. Chalmers *et al.*² in 1981 the mean age group was 59.9 years.

Gender Distribution

In present study among 75 alcoholics 89% (67/75) were males and 11% (8/75) were females. This shows an increasing trend of alcohol consumption in women also.

In a similar study conducted by D. Chalmers *et al.*² in 1981 from Harrow showed a study of 219 out of which 146 (66.66%) were men 73 (33.33) were females. In a similar study conducted by Hislop *et al.* 1983 in England male to female ratio of 2.9:1 was found. In a similar study done by T. Oduola *et al.*,¹ in Ile at Nigeria out of 200 (100%) all were men. In a study by Ray R ET AL 1988 from NIMHANS Bangalore all were 100% males.

Socio-economic Status

In the present study most of the patients 72% (54/75) belonged to lower socio-economic class and 28.% (21/75) were middle socio economic class. There is increased number of alcoholics in lower socioeconomic group (labor class) are visiting our hospitals. Being poor they tend to consume low quality drink like arrack. In a similar survey done by Wilson *et al.* in 1980 showed a high incidence in low socio-economic group.

Duration of Alcohol Intake

In our present study there were patients who consumed alcohol more than 10 years duration 62.6% (47/75) and 25% (19/75) were less than 10 years duration. In the similar study conducted by D. Chalmers *et al.*² 219/373 were severe alcoholics for more than 10 years.

Another similar study conducted by T.Oduola¹⁶ *et al.* 200 patients were studied among which 50% were moderate alcoholics consuming for less than 10 years. 50% were severe alcoholic who consumed for more than 10 years.

Presenting Complaints

In present study 60% (45/75) of patients presented with distension of abdomen. Next frequent presentation was with jaundice 40% (30/75), Bilateral pedal edema 28% (21/75), Pain abdomen 25.3% (19/75), haemetemesis 20% (15/75), malena 10.7% (8/75) breathlessness 10.7% (8/75) altered sensorium 21.3% (16/75). In a similar study done by D. Chalmers *et al.* gastrointestinal symptoms were predominant. About 60% of patients presented with duodenal ulcer and dyspepsia. 20% of patients with haemetemesis. Jaundice in 20%. Altered sensorium in 10% of patients

Haematological Manifestations Complete Blood Count

In the present study the mean hemoglobin was 9.2 gms% among moderate alcoholics and 8.5gm% among severe alcoholics' In study conducted by T. Oduola *et al.* the hemoglobin (g/dl) was 14.5 ± 1.2 among moderate alcoholics and 14.8 ± 1.2 among severe alcoholics.

In our study the total count of white blood cells were mean of 10160.84 ± 4448.65 in moderate alcoholics and 11763.9 ± 5101.30 in severe alcoholics. In the similar study

of T. Oduola *et al.*¹ WCC (mm³) was 44516.7 ± 2825.6 among moderate alcoholics and 4733.3 ± 1400.6 among severe alcoholics.

In the present study MCV in moderate alcoholics was 96.6 ± 7.77 fl. in severe alcoholics it was 104.5 ± 11.75 The highest was 110.6fl. In the same study by T. Oduola *et al.*¹ the MCV (μ m³) was 84.9 ± 9.1 in moderate alcoholics and 89.7 ± 9.7 among severe alcoholics.

In our study he MCH showed 29.00 ± 5.32 among moderate alcoholics and 27.5 ± 4.98 among severe alcoholics. In the similar study by T. Oduola *et al.*¹ MCH (pg/L) among moderate alcoholics was 28.4 ± 4.1 among severe alcoholics it was 28.9 ± 4.3 .

In present study the MCHC was 29.8 ± 4.37 among moderate alcoholics and 24.4 ± 4.30

among severe alcoholics. In the same study of T. Oduola *et al.*¹ MCHC 30.8 ± 1.8 among moderate alcoholics and 32.7 ± 0.9 among severe alcoholics.

In the present study the PCV among moderate alcoholics was 27.0 ± 7.40 and among severe alcoholics it was 28.8 ± 4.90 . In the same study conducted by T. Oduola *et al.*¹ PCV (%) 44.2 ± 3.7 among moderate alcoholics and 45.3 ± 3.8 among severe alcoholics.

Platelet count showed a mean of 190000 ± 0.69 in moderate alcoholics, in severe alcoholics the plate let count was a mean of $140000 +_0.58$. The lowest platelet count was 40,000. In the similar study by T. Oduola *et al.* the platelet count was 211733.3 ± 49906.8 among moderate alcoholics and 217966.8 ± 41736.0 among severe alcoholics. the platelet counts were above 2 lakhs normal in all groups In our study 10% of study group had thrombocytopenia out of which mean was 40,000cells/cumm. This can be the cause of transient intravascular hemolysis associated with alcoholic liver disease.³ However haematological manifestations in T. Oduola *et al.* study showed no significant changes in occasional and moderate drinkers.

Peripheral Blood Smear

In our study moderate drinkers showed normocytic normochromic anemia in peripheral blood smear. Heavy drinkers showed 30.66% of other types anemia in the peripheral blood smear.

In the similar study by T. Oduola *et al.* in severe drinkers they showed predominantly a macrocytic blood picture in peripheral blood smear. In other similar study by Latvala Jaana and Parkkila thrombocytopenia was found in 41% of alcoholics.

In addition our study along with normocytic normochromic anemia and macrocytic anemia it also showed presence of various other types of anemia like 28% showed microcytic hypochromic, 40% normocytic normochromic anemia, 8.88% dimorphic anemia, 10.66% thrombocytopenia and 4% pancytopenia. In the similar study conducted by T. Oduola *et al.* the platelet counts were above 2 lakhs normal in all groups. In our study 10% of our study group had thrombocytopenia out of which mean was 40,000 cells/cumm. In a study conducted by Latvala jaana, Parkkila 144 subjects were studied. The incidence of anemia was 51% in the alcohol abusers., ($p < 0.05$). A diverse pattern of hematological effects was observed in the alcohol abusers. In present study 60% of patients showed anemia among alcoholics. Increased mean cell volume of erythrocytes macrocytosis was seen in 60% of alcoholics $p < 0.006$. In our study 26.6% of alcoholics showed macrocytes in peripheral blood smear. In a similar study done by H. Koivisto, J. Hietala, P. Anttila⁴ out of 105 alcoholics 60% showed macrocytes in blood smear.

Bone Marrow Aspiration Study

In our study abnormalities of bone marrow shows moderate alcoholics 23 and 21 severe alcoholics. Among them Erythroid hyperplasia is seen 10.6% of moderate alcoholics and 2.6% in severe alcoholics. In addition our study 6.6% of Megaloblastic picture seen in moderate alcoholics, 9.3% in severe alcoholics. Sideroblastic picture 1.3% in moderate alcoholics and 6.6% in severe alcoholics. Vacuolation RBC 5.3% and 4% in severe alcoholics. In the similar study conducted by Latvala Jaana and Parkkila bone marrow study revealed vacuolization of pro- normoblasts in 24% of the alcoholic patients. Megakaryocytes in the cell periphery were also vacuolized in 20% of the alcohol abusers. The bone marrow abnormalities were related to the duration of alcohol intake.

In our study out of 44 patients who had abnormal bone marrow 30.6% were moderate alcoholics 28% were severe alcoholics. In a similar study done by J. Latvala., Melkko, and O. Niemelä out of 138 consecutive adult patients undergoing bone marrow aspiration due to macrocytosis 49% were severe alcoholics and 20% were moderate alcoholics. Bone marrow aspirates from 12 alcoholic patients showed vacuolization of pro-normoblasts and the presence of ring sideroblasts were noted in 8 cases. In a similar study done by Shinji Nakao, M.D. Mine Harada from Japan in 1990 showed thrombocytopenia 5% in severe alcoholics.

In our present study liver function tests shows that abnormal LFT 30/75 (40%) of alcoholics. The total bilirubin raised in both moderate and severe alcoholics. $P < 0.000$. *S Direct bilirubin raised more in severe

alcoholics as compared with moderate alcoholics. $P < 0.003$. *S The proteins levels are very low in severe alcoholics and albumin levels are very low, as compared with moderate alcoholics. SGOT & SGPT is more elevated in severe alcoholics. ALP is significantly raised in severe alcoholics. $P < 0.0006$ *S. In the similar study done by "Niemela O in Biomarkers in alcoholism shows the laboratory findings elevations of serum γ glutamyl transferase, alkaline phosphatase and bilirubin levels. Up to 70% of patients with moderate to severe alcoholic hepatitis already have cirrhosis identifiable on biopsy examination at the time of diagnosis.⁵ another similar study by Menon KV, Gores GJ, Shah VH of all chronic heavy drinkers, only 15–20% develop hepatitis or cirrhosis, which can occur concomitantly or in succession.⁶

Summary

1. In this study period of one years between July 2016 to July 2017, 75 adults patients were alcoholics taken for study. These patients were admitted at mahatma Gandhi Memorial Hospital Warangal.
2. Among 75 alcoholics, 49 were moderately alcoholics and 26 were severe alcoholics.
3. Among these 75 alcoholics 67 (89%) were males and 8 (11%) were females.
4. The age group of study people ranged from 20 to 60 years
5. The maximum incidence of alcoholics were in the age group 31-50 years (51/75) 68. Alcoholism was uncommon below 20 years and above 60 years.
6. 72% of patients belonged to low socio-economic group and 28% belonged to middle socio-economic group.
7. The presenting complaints included distension of abdomen in 60% (45/75) of patients. Next frequent presentation was with jaundice (30/75) 40%, Bilateral pedal edema 28% (21/75), Pain abdomen 25% (19/75), haemetemesis 20% (15/75), malena 10.6% (8/75), breathlessness 2 1% (16/75) and altered sensorium 21% (16/75).
8. On physical examination 45/75 (60%) of alcoholics had pallor. Icterus was present in 30/75 (40%), pedal edema was present in 21/75 (28%), Clubbing was present in 15/75 20%, Parotid swelling was present in 24% (12/75), Other features of liver cell failure like loss of axillary hair, dupuytren's contracture, breast atrophy and testicular atrophy were seen in 19/75 (25%) of alcoholics.
9. Per abdomen findings showed hepatomegaly was present in 40/75 (53%) of alcoholics. Spleenomegaly was present in 5/75 (6.6%), with ascitis 10/75 (13%)
10. 60% of the alcoholics had anemia. The mean haemoglobin was 9.2 gms% among moderate

alcoholics and 9.0gm% among severe alcoholics.

11. The total counts of white blood cells were mean of 10160.8 ± 4448.65 cells/mm³ in moderate alcoholics and 11763.9 ± 5101.30 cells/mm³ in severe alcoholics. The lowest count was 3900 cells/mm³ and the highest count was 20,700 cells/mm³.
12. The mean MCV in moderate alcoholics was 96.6 ± 7.77 fl. In severe alcoholics it was 104.5 ± 11.75 fl, the highest was 110.6 fl.
13. Platelet count showed a mean of $1.9.00 \pm 0.69$ cells/mm³ in moderate alcoholics in severe alcoholics the platelet count was a mean of 1.40 ± 0.58 . The lowest platelet count was 40,000 cell/mm³.
14. Peripheral blood smear 45/75 (60%) showed all types of anemia. Normocytic normochromic anemia was present in 18/45 (40%) of patients. Next predominant was microcytic hypochromic anemia which was present in 12/45 (28%) of patients. Macrocytic anemia was present in 11/45 (26.6%) patients. Dimorphic anemia was present in 4/45 (8.88%).
15. In the present study 31/75 (41%) showed normal bone marrow in both alcoholics. Abnormal bone marrow picture was seen in 44/75 (59%) patients. Among which megaloblastic picture was seen in 12/44 (27.4%) of alcoholics. Erythroid hyperplasia was seen in 10/75 (13%) of alcoholics. Vacuolated RBC was seen in 7/75 (9.3%). Sideroblasts was seen in 6/75 (8%) of alcoholics. 9 patient showed myelodysplastic marrow.

CONCLUSION

- Alcoholism was present in both men and women. More common among men.
- Alcoholism was common in middle aged group.
- Alcoholism predominately persisted in low socio economic group.
- Anemia is the predominant feature among chronic alcoholics. Anemia was independent of bleeding, Severity of anemia appear to be related to the severity of alcohol intake.
- There is an increased risk of cirrhosis and infection among alcoholics.

- Microcytic hypochromic, macrocytic anemia and all types of anemia can be seen in alcoholics.
- Bone marrow studies reveal predominantly megaloblastic picture. Other features seen were increased vacuolization in pro-normoblasts precursors of red blood cells, megaloblastic picture and Erythroid hyperplasia Sideroblastic and Myelodysplastic picture was also seen.
- Macrocytes was also prominent seen in peripheral blood smear.
- Thrombocytopenia was also a feature of chronic alcoholics.
- Hematological manifestations are reversible with cessation of alcohol
- Early detection of anemia among alcoholics can prevent further complications of anemia like failure and reduce the mortality in lower socioeconomic group of people.
- There also abnormality in liver function test like elevated serum bilirubin lower levels of Albumin, SGOT, SGPT and also elevated ALP in chronic alcoholics.

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Primary Tuberculosis of Glans Penis - Mimicker of Malignancy: A Case Report and Review of Literature

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Abstract

Tuberculosis (TB) of penis is a rare form of genitor-urinary TB. It usually presents as an ulcerative or a nodular lesion. Most of the times, the diagnosis is delayed either due to a delay in onset of voiding difficulty or being masked by the presence of phimosis. In this case report, we present a case of a 65-year-old male presenting with ulcerative lesion involving the glans penis, mimicking a carcinoma. Biopsy confirmed TB and the lesion disappeared with antitubercular therapy. The purpose of this manuscript is to highlight the rarity of the disease and also to stress on the fact that not all ulceroproliferative lesions of the penis are malignant. Prompt diagnosis and appropriate treatment and a high index of clinical suspicion can to a large extent obviate the need for an ablative penectomy.

Key words: Antitubercular therapy, Phimosis, Penis, Tuberculosis

INTRODUCTION

Primary tuberculosis (TB) of glans penis is an extremely rare condition. With active implementation of Global TB Eradication Programme by the World Health Organization (WHO), and by its "STOP TB" campaign, the WHO has been taking all possible efforts to eradicate TB by 2050.^[1] The overall incidence of TB penis is on the decline. With an ever-increasing awareness among the public and patients, the overall incidence of TB penis has further declined in the current era.^[2]

CASE REPORT

A 65-year-old male presented with ulcerative lesion of glans penis of 4 months duration. The growth was

slow growing and insidious in onset and was painful. Over the past 2 months, he noticed whitish discharge from the growth surface that foul smelled. He did not have any voiding difficulties. His wife was on treatment for pulmonary TB for the past 6 months. However, he denied having coitus for the past 3 years. Figure 1 describes the ulcerative lesion at the time of presentation. Figure 2 shows the lungs and kidneys to be free from the disease.

On examination, an ulcerative lesion with surrounding erythema and induration was found over the glans penis. There was a foul-smelling purulent discharge from the surface of the lesion. The prepuce was densely adherent over the glans penis, which bled even on gentle separation. A dorsal slitting of the prepuce was done and an edge-wedge biopsy taken from the lesion.

Figure 3 illustrates the microphotograph of the biopsy specimen in low and high power. The section revealed skin with ulceration and abscess formation of subcutaneous tract with abscess lined by granulomas comprised epithelioid cells, Langhans' giant cells, and a dense cuff of lymphocytes. Three consecutive urine smear for acid-fast

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bacilli (AFB) and urine for AFB culture were found to be negative. A diagnosis of primary TB of the penis was made, and the patient was started on antituberculous therapy (ATT). He was given four drugs including isoniazid, rifampicin, pyrazinamide, and ethambutol for 2 months and rifampicin and isoniazid for the next 4 months.

Following 8 weeks of ATT, the lesion almost completely regressed. The erythema surrounding the ulcerative lesion completely disappeared and the pain also disappeared. Figure 4 depicts the post-treatment images, where the lesion and the induration had completely vanished.



Figure 1: Pre treatment image showing the lesion

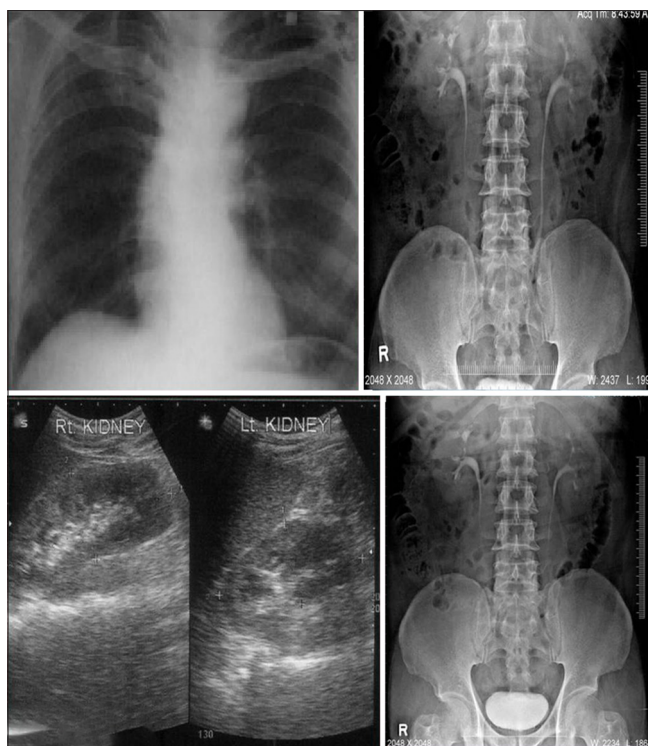


Figure 2: Imaging showing the chest and kidneys to be free from tuberculosis

DISCUSSION

TB is a major health problem. It is the most widespread and persistent human infection in the world. This can affect any organ and can mimic any illness, and hence, it is called, “a great mimicker.”^[3] Millions of people are affected by TB every year, and it ranks alongside human immunodeficiency virus as a leading cause of death worldwide.^[4]

TB of penis presents as lesions in the glans or shaft of penis. It constitutes to <1% of all cases of TB of genitalia in males.^[5] Fournier is considered to have first described the disease in 1848, where the patient had multiple ulcerative lesions of the penis, with regional lymphadenopathy.^[6] TB of penis can be classified into two broad types: Primary and secondary. Secondary TB of penis occurs along with evidence of pulmonary TB elsewhere and occurs by hematogenous dissemination from other primary localizations.^[7] Primary TB, on the other hand, occurs traditionally as sequelae of ritual circumcision, where the operator sucks the circumcised penis. Sucking was done as a hemostatic and a styptic measure. Some of them had open TB and had readily transmitted the infection onto the circumcised penis.^[8] Such measures have practically been eliminated in current practice, and the overall incidence has significantly come down in the past two decades. Primary TB can also occur due to coital contact with the disease already present in

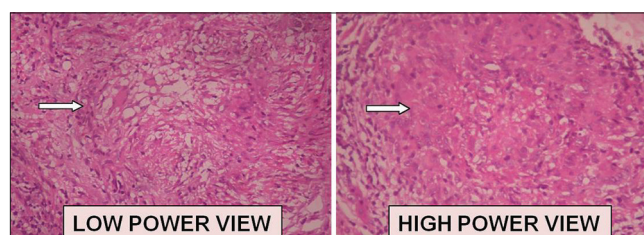


Figure 3: Microphotograph showing skin with ulceration with abscess formation of subcutaneous tract



Figure 4: Post treatment image showing a complete resolution of the lesion

the female genitalia or from the clothing that is infected with tubercle bacilli.^[9]

There also exists a confusion regarding the exact nomenclature of penile TB. Various other classifications for TB penis are also being proposed and the common ones include true TB, penile tuberculide, papulonecrotic tuberculide, and ulcerated lupus vulgaris.^[10] Many a time, demonstration of AFB may not be possible in the biopsied specimen and a decision to call it TB may purely be based on rest of the corroborative findings such as epithelioid granulomas and Langhans' giant cells. Ramesh *et al.* have stated that it becomes difficult to distinguish tuberculides from other forms of cutaneous TB. Hence, lesions localized to the glans penis may be more appropriately referred to as "TB of glans penis."^[11]

TB of penis characteristically affects the skin, glans, or corpora cavernosa. Most of them are ulcerative as in our case or rarely may present as an isolated nodule or papulonecrotic tuberculides.^[12,13] Unless the possibility of TB affecting this organ is thought of, it is often likely to be missed in clinical practice. This condition responds well to medical management with ATT, and the lesion is expected to regress well with conservative measures.

The purpose of this case report is to highlight that a prompt diagnosis, appropriate treatment, and a high index of

clinical suspicion could to a large extent obviate the need for an ablative procedure in the form of partial penectomy.

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Placenta Percreta with Urinary Bladder Infiltration: A Modified Posterior Approach - A Case Report and Lessons Learnt

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Abstract

Placenta percreta can be one of the life-threatening obstetric emergencies. Placenta percreta involving the urinary bladder is one of the acute obstetric conditions where the urologist plays a major role in stabilizing the general condition of the patient. In this case report, we present a case of a 28-year-old female, who had a premature delivery at 32 weeks of gestation. This patient continued to have persistent bleeding per vaginum and had frank hematuria, which did not settle down with bladder wash and other forms of conservative management. A modified posterior approach hysterectomy and a partial cystectomy along with the residual placental mass were carried out, following which the mother and the child were stable. The purpose of this manuscript is to highlight the rarity of such a condition and also to stress on the fact that one should be vigilant in having a high index of clinical suspicion in anticipating profuse bleeding following a delivery. Prompt diagnosis and a proactive approach would enable an appropriate treatment for this, otherwise, potentially lethal disease.

Key words: Cystectomy, Hematuria, Placenta percreta, Placenta previa

INTRODUCTION

Placenta percreta is a complication of pregnancy that can sometimes be life-threatening for both mother and fetus. Three forms of abnormal surface formation between the placenta and the uterus are demonstrated: Placenta accreta, placenta increta, and placenta percreta.

As a result of an inadequate development of the decidua, there is an abnormal connection between the trophoblast and the myometrium; in cases of placenta accreta, the chorionic villi grow into the basal decidua; in placenta increta, the chorionic villi penetrate into the musculature,

and in placenta percreta, the villi pass through the myometrium. Infiltration of not only the serosa but also of other neighboring organs such as the urinary bladder and large bowel can occur and serious complications may arise. Here, we present one such case where there is a severe postpartum bleeding and hematuria, necessitating hysterectomy, and partial cystectomy.

CASE REPORT

A 28-year-old female, who had previously undergone a cesarean delivery in 2007 and dilatation and curettage in 2008, was admitted to the labor ward at 32 weeks of gestation with a history of a sudden severe painless vaginal bleeding from a sonographically diagnosed placenta percreta [Figure 1]. An immediate cesarean section was performed and a live male infant weighing 1.5 kg was delivered. The placenta was found adherent to the lower uterine segment and attempts at removal caused torrential bleeding.

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As the bleeding continued, urologists were called for and bilateral internal iliac artery ligation was done. Even after ligation of internal iliac vessels, there was persistent bleeding from vagina and from the bladder resulting in clot retention. Cystoscopy could not be done and bladder wash was ineffective. Hence, a vesicotomy was performed. The blood clots were removed; both ureteric orifices were identified and Double J stenting was done. There was a huge mass in the supratrigonal region, which was protruding from the posterior wall of the bladder, with active bleeding from the surface. Attempts to pack betadine soaked ribbon gauge and dissection of the bladder from the lower uterine segment were unsuccessful. As the diagnosis of placenta percreta with involvement of the urinary bladder was made preoperatively, such a catastrophe was anticipated in advance and a modified posterior approach hysterectomy was carried out. By a modified posterior approach, hysterectomy and a partial cystectomy along with the residual placental mass were carried out.

This technique consists of posterior entry of the vagina, lateral retraction of the ureters, and sequential ligation of parametria medial to the ureter. Finally, the adherent portion of the bladder was resected (partial cystectomy), with uterus and bladder being repaired in two layers with bilateral stents, suprapubic, and urethral catheters placing *in situ*. Intraoperatively, the patient needed multiple units of packed cells and fresh frozen plasma.

Histopathological evaluation revealed placenta percreta with invasion of trophoblastic tissue through the wall of the lower uterine segment and involving the bladder base [Figure 2].

The stents and catheters were removed 2 weeks later. The mother and child are doing well at present.

DISCUSSION

Placenta is an intermediary organ that attaches itself to the uterus on one side and is connected to the fetus on the other side. This serves as a vital organ to allow an exchange of gases, eliminate waste products, and effectively supply nutrients to the fetus. Placenta accreta involves a primary deficiency of decidualized endometrium allowing excessive trophoblastic invasion directly onto or into the myometrium.^[1] Placenta accreta adheres to the myometrial surface. When the placenta invades the myometrium, it is called as placenta increta. The most severe scale of abnormal placental attachment is called as placenta percreta, where the extravillous trophoblasts invade beyond the full thickness of the myometrium and possibly into other intra-abdominal organ structures, usually the bladder.^[2]

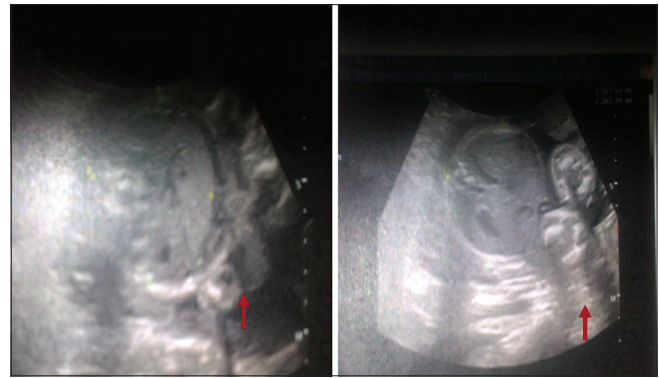


Figure 1: Sonographic appearance of placenta previa

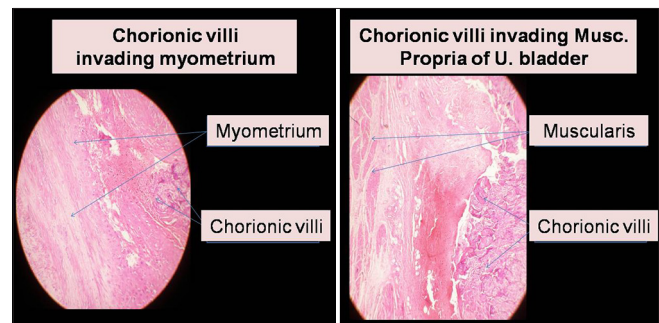


Figure 2: Microphotograph with H & E stain, showing invasion of chorionic villi into myometrium and urinary bladder

The overall incidence of placenta accreta, increta, and percreta vary between 1:540 and 1:93,000. The average incidence is ~1:7000.^[3] The various factors that can predispose to an abnormal placental location include prior cervical dilatations and curettages, endometritis, submucous myomas, and uterine scars.

Clark *et al.* studied the causal relationship between abnormal placentation and previous cesarean section. In their study, they observed that the spongy decidua cannot be found and the myometrial vessels that are well perfused might open up, resulting in torrential bleed and shock. Prompt diagnosis and appropriate treatment are, therefore, of paramount importance.^[4]

In patients who have undergone previous cesarean sections, one should always be aware of the correlation of placenta previa with abnormal placentation. Of course, placenta percreta can also occur during first pregnancies without any prior gynecological operations or endometritis.

Sonography, to a certain extent, can localize the status of the placenta.^[5] Finberg *et al.* laid down certain sonographic criteria that could very well suggest placenta accrete. These are the absence of a normal, hypodense retroplacental myometrial zone, a reduced or absent surface between uterine serosa and urinary bladder, and, possibly, the presence of focal exophytic tissue.^[6] Doppler

sonography can detect an abnormal vascularization of the myometrium.

Magnetic resonance imaging (MRI) can be used as a supplementary diagnostic procedure in cases where the placenta cannot be adequately evaluated by sonography and/or when there is an elevated risk of abnormal placentation.^[7] Lim *et al.* correlated the probability scores of placenta accreta on magnetic resonance imaging with hemorrhagic morbidity and concluded that the probability scores for antenatal placental MRI may not be associated with increasing degrees of hemorrhage.^[8]

A further sign of a placenta accreta/increta/percreta may be an otherwise bizarre elevation of alpha-fetoprotein (AFP) levels in the maternal serum. There is a significant relationship between placenta accreta/increta/percreta and elevated AFP levels in maternal blood.^[9,10] When macroscopic hematuria is found, an infiltration of the urinary bladder must be considered. If placenta percreta is suspected, then a pre-operative cystoscopy is recommended as a planning aid for the necessary operative steps.^[11] In the present case, there was no macroscopic hematuria so this diagnostic step was not performed.

The therapy of choice for placenta percreta is hysterectomy. Bilateral ligation of the internal iliac arteries offers a possibility to reduce blood loss during the hysterectomy. Various authors have described balloon catheter occlusion of the iliac vessels in patients with placenta percreta. The catheter is implanted preoperatively and inflated, after delivery of the baby, during the hysterectomy.^[12]

With percreta, subtotal hysterectomy is to be avoided since most arteries remain uncontrolled and reoperation rates are high, approximately 90%.^[13] A modified approach to hysterectomy is recommended. With this fashion, the uterus is mobilized until the only remaining attachment is where the placenta percreta has invaded the bladder. The involved portion of the bladder is then resected with hysterectomy specimen followed by bladder reconstruction.^[14]

CONCLUSION

Placenta percreta with bladder invasion is a major contribution to maternal morbidity and mortality. This particular case is of great importance for the urologist, as the condition is quite rare and many a time, the urologist is caught unaware of this potentially lethal entity, where internal iliac artery alone is not adequate. A high index of clinical suspicion is mandatory in such situations. We present this case to stress out the importance of early recognition of this life-threatening condition and to have a good maternal and neonatal outcome.

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