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Original Article

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Occurrence of Painful Diabetic Peripheral Neuropathy among Type 2 Diabetic Patients Attending a Tertiary Care Hospital

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Abstract

Introduction: Diabetes affects 382 million people worldwide, and its prevalence is expected to increase to 592 million by the year 2035. Painful diabetic peripheral neuropathy (PDPN) is a common type of diabetic neuropathy and the most common cause of neuropathic pain. Hence, there is a need to access the incidence and the prevalence of this condition. The incidence of diabetes and its complications has increased to a greater extent among the rural population which have to be concentrated as there are lesser studies available for that population groups.

Materials and Methods: Incidence is tested by a cross-sectional descriptive study consisting of two phases: Phase 1, an initial screening questionnaire including one question about pain; Phase 2, neurological history and examination using the Toronto Clinical Scoring System (TCSS). The observations thus obtained are evaluated with suitable statistics tool (SPSS version 16), and results are represented in the form of figures and graphs.

Results: Total number of subjects were 100 of them 59 were male and 41 were female. Diabetic age of the individuals ranges between 2 and 19 years. The highest score with TCSS was 13 and least was 3. More than 86% of the subjects were suffering from peripheral neuropathy among which 46% are with mild and 35% with moderate and 5% with severe grades of DPN. Incidence of PDPN was increasing rapidly with the raising fasting blood sugar (FBS) levels and was 100% with FBS levels more than 261 mg/dl.

Conclusions: PDPN incidence among the diabetic individuals is relatively high in the study population. Age does not influence the occurrence of PDPN among the diabetics while the diabetic age of the individuals has a highly significant relation with the occurrence of PDPN. The occurrence of PDPN was more among the individuals with high FBS levels which indicate the necessity of controlled glycemic levels in the prevention of complications associated with diabetes mellitus.

Key words: Neuropathic pain, Painful diabetic peripheral neuropathy, Rural population, Toronto clinical scoring system

INTRODUCTION

Diabetes affects 382 million people worldwide, and its prevalence will be increasing to 592 million by the year 2035.[1] Diabetic peripheral neuropathy (DPN), also known as distal symmetric polyneuropathy, is a well-known, long-term complication of diabetes which occurs in 30-50% of patients with the disease[2] and is associated with a higher rates of morbidity and mortality.[3] Members of an International Consensus Meeting on the outpatient diagnosis and management of DPN agreed on a simple definition of diabetic neuropathy as "the presence of symptoms and/or signs of peripheral nerve dysfunction in people with diabetes after the exclusion of other causes."[4]

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Diabetic neuropathy can have a number of clinical or subclinical presentations. Painful diabetic neuropathy

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(PDN) is a common type of diabetic neuropathy and the most common cause of neuropathic pain.[5] PDN symptoms exhibit a symmetrical "stocking and gloves" distribution and have frequent nocturnal exacerbations. It can present from a mild pins and needle sensation to stabbing, burning, unremitting, or even unpleasant electric shock sensation. Allodynia in the form of cutaneous hypersensitivity leading to acute distress on contact with an external stimulus, such as clothing can also occur.[6] The pain is often worse at night and often disturbs sleep, causing tiredness during the day. This may be so painful that the performance of daily activities is disturbed, thereby impacting their employment and social life. The constant, unremitting pain and withdrawal from social life often result in depression symptoms.[7] In the severe cases, patients lose their appetite and experience significant weight loss, which is reported in the literature as "diabetic neuropathic cachexia."[6]

It was quoted in a recent review[8] that knowledge of the epidemiology of painful DPN (PDPN) "is compromised by the lack of large population-based studies and by the lack of agreement by authorities on diagnostic criteria, precise definitions, and grading of severity of PDPN. These problems can lead to potentially important sampling biases and measurement error." Furthermore, the incidence of diabetes and its complications were increased to a greater extent among the rural population. Incidence is tested by a cross-sectional descriptive study consisting of two phases: Phase 1, an initial screening questionnaire including one question about pain; Phase 2, neurological history and examination using the Toronto Clinical Scoring System (TCSS). Subjects with peripheral neuropathy completed the neuropathic pain scale (NPS) to assess severity and nature of the pain. The observations thus obtained are evaluated with suitable statistics tool (SPSS version 16) and results are represented in the form of figures and graphs.

MATERIALS AND METHODS

The study was approved by the local Ethics Committee and written informed consent was obtained from each patient.

Study Design

It is a study done in a clinical setting in two phases. Phase 1 an initial screening questionnaire including one question about pain; Phase 2, neurological history and examination use the TCSS. Subjects with peripheral neuropathy completed the NPS to assess severity and nature of the pain and impact on quality.

Study Duration

The study was conducted during the months of June and July of 2014.

Study Population

The subjects are the Type 2 diabetic patients visiting our outpatient unit of General Medicine Department of our institute.

Sample Size and Selection Criteria

The sample size is 100. The criterion for selection is those who were suffering from Type 2 diabetes for more than 2 years.

Exclusion Criteria

Subjects with Type 1 are excluded from the study. Subjects who have other possible causes for having peripheral neuropathy are excluded from the study.

Data Collection Procedures and Instruments

Phase 1: Primary survey

All eligible subjects are given instructions about the research and are requested to answer screening questionnaire. The latter included the question, "Do you have a burning, aching or tenderness in your legs or feet?" This was taken from the diabetic neuropathy symptom score. Subjects were also asked the year of diagnosis of diabetes.

Phase 2: Clinical examination and further assessment

Those eligible subjects from Phase 1 of the study were enrolled in the second phase, in which a clinical neurological history and examination were carried out by one observer (M.D.) who assessed the presence and severity of PDPN. Peripheral neuropathy was assessed using the validated TCSS.[9] Subjects with peripheral neuropathy completed the NPS by which the sensation of pain is categorized into neuropathic and non-neuropathic.

RESULTS

Sex Distribution

Total number of subjects in the present study was 100. The majority of these patients in present study were males 59% (59 males). 41 patients were females (41%) (Figure 1).

Age Distribution

Regarding age distribution least age of the individual was 33 years and the highest was 71 years.

The majority of the patients in the present study were between age groups of 51 and 60 years (40%) (Figure 2).

Duration of Diabetes

Diabetic age of the individuals ranges between 2 and 19 years. 55 patients in the present study had duration of diabetes between 2 and 5 years which constituted the majority (Figure 3).

Type of Medication

About 76 patients in present study were using only oral hypoglycemic drugs. 24 patients in the present study were using both oral hypoglycemic drugs and insulin preparations (Figure 4).

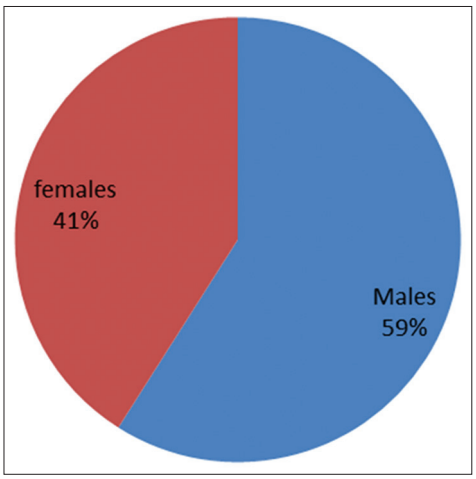

Figure 1: Sex distribution

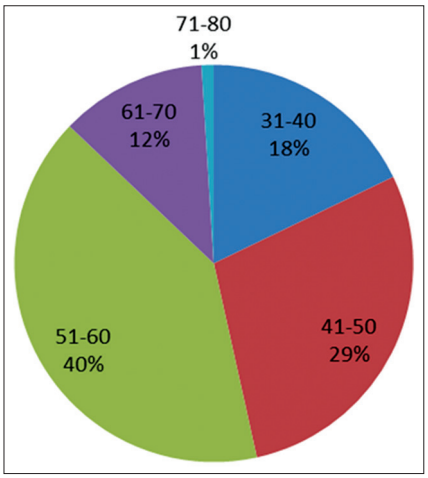

Figure 2: Age distribution

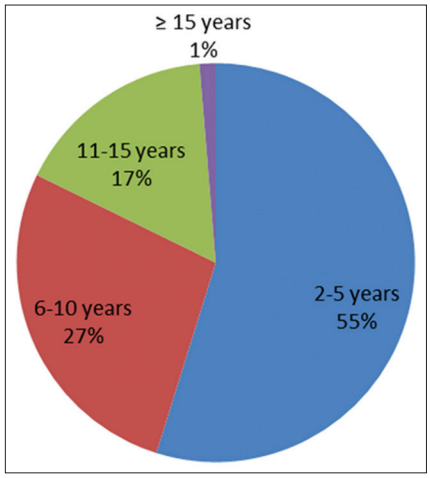

Figure 3: Duration of diabetes

Fasting Blood Sugar (FBS) Levels

FBS levels among the subjects least observation was 100 mg/dl, and the highest was 377 mg/dl. The majority of the patients had FBS levels between 100 and 160 mg%. 23% had FBS levels between 161 and 210 mg% (Figure 5).

Diabetic Neuropathy Grading

14 patients had no diabetic neuropathy. The majority (46%) had mild neuropathy; 35% had moderate neuropathy and 5% had severe neuropathy. The highest score with TCSS was 13 and least was 3 (Figure 6).

Severity of Neuropathic Pain

28 patients had non-neuropathic pain. 27% had mild neuropathic pain. The majority (33%) had moderate neuropathic pain. 27% had mild neuropathic pain. 12% had severe neuropathic pain. NPSS score ranges between 2 and 9 (Figure 7).

Prevalence of PDPN

79 patients had PDPN. 21 patients had no PDPN (Figure 8).

Correlation of PDPN with Age

There was no positive correlation of age with occurrence of PDPN in the present study (Figure 9).

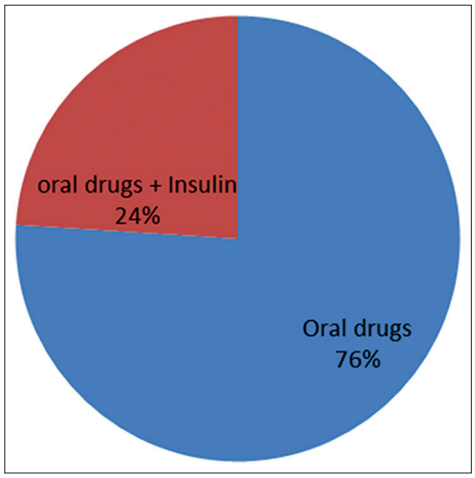

Figure 4: Type of medication

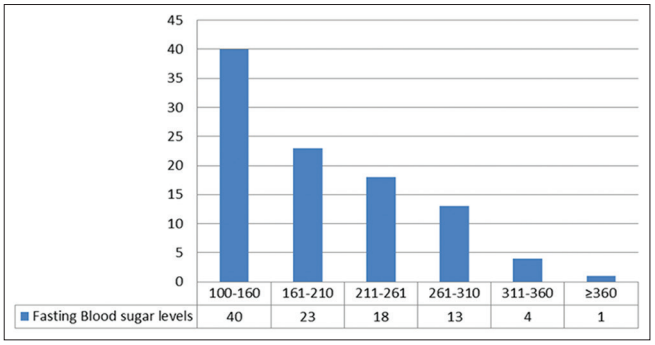

Figure 5: Fasting blood sugar levels

Correlation of PDPN with Duration of Diabetes

There was positive correlation between occurrence of PDPN and duration of diabetes. As the duration of diabetes increases, there is a steady increase in the occurrence of PDPN. Patients with duration of diabetes of more than 15 years had 100% occurrence of PDPN (Figure 10).

Correlation of PDPN with FBS Levels

In the present study, the occurrence of PDPN was increasing with the increasing fasting blood glucose levels and was 100% with FBS levels more than 261 mg/dl (Figure 11).

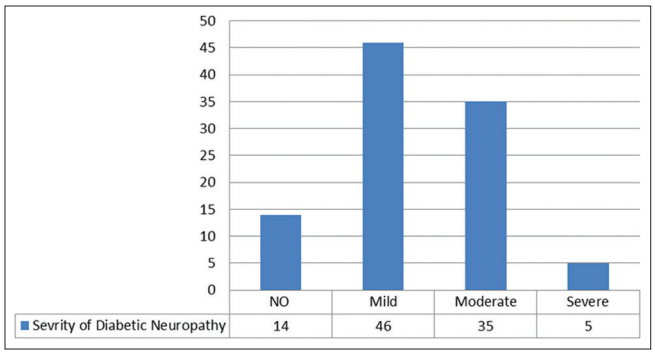

Figure 6: Grading of diabetic neuropathy

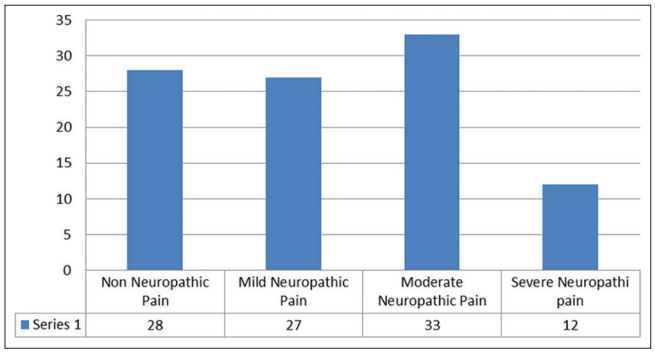

Figure 7: Severity of pain

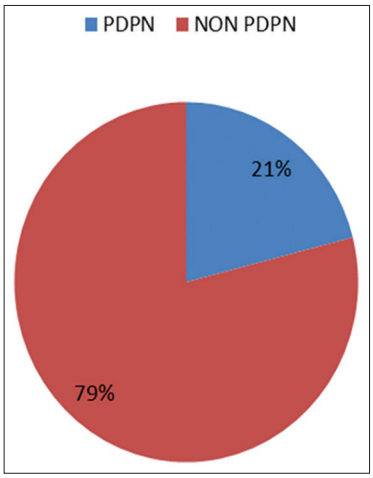

Figure 8: Prevalence of painful diabetic peripheral neuropathy

DISCUSSION

On observation of results, more than 86% of the subjects were suffering from peripheral neuropathy among which 46% are with mild and 35% with moderate and 5% with severe grades of DPN. Among the total subjects, 72% are with neuropathic pain among which severity is mild in 27%, moderate in 33% and severe in 12% of the individuals. Among the total subjects nearly three-fourths were suffering from PDPN, which is very much higher than that of the literature available both in India and among other parts of the world.[10,11] There is no much influence of age among the diabetics in the occurrence of PDPN. But with the increase in diabetic age the occurrence of PDPN

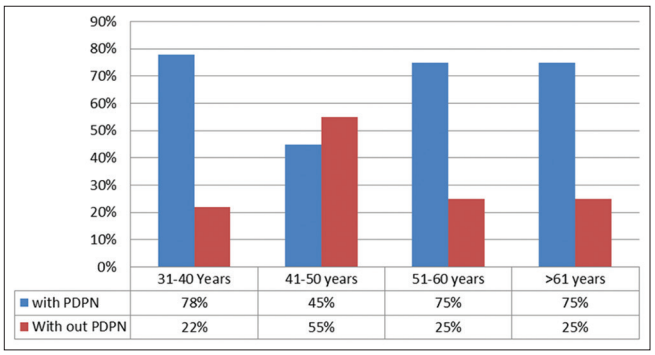

Figure 9: Painful diabetic peripheral neuropathy versus age

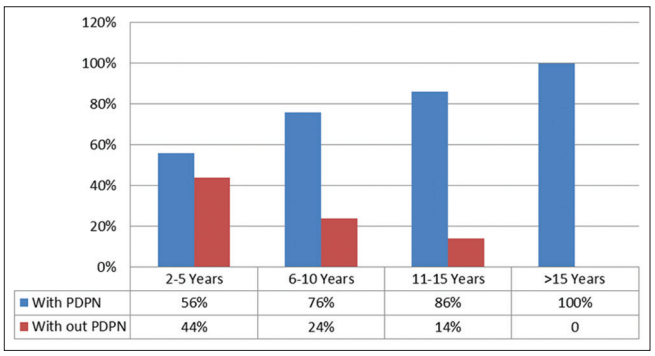

Figure 10: Painful diabetic peripheral neuropathy versus duration of diabetes

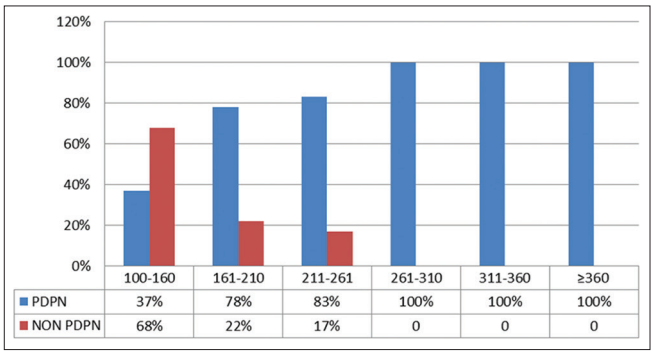

Figure 11: Fasting glucose level versus painful diabetic peripheral neuropathy

among the subjects was increasing with diabetic age and was 100% in the individuals with a diabetic age of more than 15 years. These results were in par with the other published studies.[10,11] On observing the trends of occurrence with the fasting blood glucose levels, incidence was increasing rapidly with the FBS levels and was 100% with FBS levels more than 261 mg/dl. Though these results were in par with the ongoing studies, cohort study has to be done to know about the relation of blood glucose levels with the occurrence of PDPN.

CONCLUSION

From the above discussion, it can be concluded that PDPN incidence among the diabetic individuals is relatively high in the study population. Age doesn't influence the occurrence of PDPN among the diabetics while the diabetic age of the individuals has a highly significant correlation with the occurrence of PDPN. The occurrence of PDPN was more among the individuals with high FBS levels which indicate the necessity of controlled glycemic levels in the prevention of complications associated with diabetes mellitus.

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Original Article

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Renal Arterial Doppler in Acute Ureteric Obstruction: A Prospective Study

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Abstract

Introduction: Acute renal colic due to ureteric obstruction is one of the leading causes of morbidity.

Aims and Objectives: To study arterial Doppler waveform alterations in patients with acute ureteric obstruction presenting with or without dilatation of the pelvicalyceal system. To evaluate and compare the resistive indices (RI) in unilateral obstructed kidney with the contralateral non-obstructed kidney taken as control, with final diagnosis established by computed tomography (CT).

Materials and Methods: A prospective study was carried on 60 patients who are referred to the Department of Radiodiagnosis, Vydehi Institute of Medical Sciences and Research Centre, Bengaluru with a history of acute renal colic from December 2010 to June 2012 (18 months). Patients were subjected to gray scale ultrasonography followed by renal arterial Doppler studies. The final diagnosis was based on CT.

Results: The mean RI in obstructed kidneys was significantly higher than in non-obstructed kidneys (0.72 vs. 0.63; $P < 0.001$). The distal obstruction showed more RI value of 0.72 ± 0.05 than proximal obstruction RI value 0.7 ± 0.04. Both peak systolic velocities and end diastolic velocities were reduced in obstructed kidney in comparison to contralateral normal kidney, and the differences in velocities were statistically significant.

Conclusion: Renal arterial Doppler is a useful diagnostic modality and can be used as a supplemental tool in the evaluation of patients with acute renal obstruction.

Key words: Acute ureteric obstruction, End diastolic velocity, Peak systolic velocity, Renal Doppler, Resistivity indices

INTRODUCTION

Acute renal colic due to ureteric obstruction is one of the leading causes of morbidity.[1] Ureteric obstruction predisposes to urinary infection, renal damage, and failure. Gray scale ultrasonography (USG) though useful in the diagnosis of hydronephrosis fails to reveal the acute obstruction of the kidney in 35% of the cases.[2] Even with meticulous technique, USG fails to detect obstruction in a very small proportion of patients, when pelvicalyceal system (PCS) dilatation is not detected due to diuresis resulting from underlying renal parenchymal disease, dehydration, intermittent obstruction by calculus, and decompression of the PCS occurring due to calyceal fornix tear.[1] Intravenous urography (IVU) or computed tomography (CT) urography is the gold standards for demonstrating acute ureteric obstruction.[2] Both these modalities involve radiation, which may not be desirable in patients, especially those who present with multiple episodes of renal colic.

Whenever there is complete acute ureteric obstruction due to calculus, there will be changes in the renal blood flow with associated elevation in renal pelvic pressure.

In the initial few hours, there will be dilation of afferent arterioles, leading to increase in blood flow. After 5 h, there will be a subsequent decrease in the flow likely due to the

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action of prostaglandins and other vasoactive substances on the afferent arterioles.[3] This reduced renal flow can last for more than 24 h, even when the pelvic calyceal pressure is returning toward normal.

The pathophysiological changes that occur due to reduction in renal blood flow due to obstruction by the calculus can be conveniently demonstrated by using Doppler USG parameter, that is, resistive index (RI) wherein the RI will increase after 6 h of obstruction and will attain its peak between 6 and 48 h, with minor fluctuations thereafter.[4]

In a study conducted by Platt *et al.*,[5] they have observed that whenever there is a PCS obstruction, the observed RI was >0.7 as compared to non-obstructed PCS with RI <0.7.

Aims and Objectives

1. To study renal arterial Doppler waveform alterations in patients in acute renal obstruction presenting with or without dilatation of the PCS
2. To evaluate and compare the RI in acute renal obstruction with the normal contralateral kidney taken as control, with final diagnosis established by CT.

MATERIALS AND METHODS

A prospective study is carried on 60 patients who are referred to the Department of Radiodiagnosis, Vydehi Institute of Medical Sciences and Research Centre, Bengaluru with a history of acute renal colic from December 2010 to June 2012. All patients with a history of acute renal colic (<24 h) and subsequently found to have urinary calculi by CT were included. Pregnant females in whom right sided pelvicalyceal dilatation is a physiologic entity, patients with bilateral outflow tract obstruction due to benign prostatic hyperplasia, patients with bladder tumors, urethral stricture, medical renal disease, diabetes, and hypertension were excluded.

The selected patients were subjected to gray scale USG and Doppler evaluation of renal arteries done. The kidney on the side of obstruction was treated as the case, and the contralateral normal (unobstructed) kidney served as the control.

All patients are subjected to USG and Doppler in HD 15, Philips, India using a 3.5-5 MHz transducer. Presence or absence of PCS dilatation was assessed in each kidney on the gray scale images. The machine calculated the RI, which is derived from the three Doppler spectra obtained from upper, mid, and lower interlobar arteries, and the mean RI is taken. The renal RI could also be calculated manually as follows: (Peak systolic velocity-end diastolic velocity)/peak systolic velocity. Δ RI is determined as the difference in RI of the corresponding kidney and normal contralateral kidney.

CT is done for confirmation of calculus causing obstruction using General Electric Medical system 16 slice multidetector row CT equipment. Non-enhanced CT scan of the abdomen is performed extending from the dome of the diaphragm to iliac crest with 5 mm spiral sections followed by 1.25 mm reconstruction. CT scan was used to detect PCS dilatation if any, the obstructing calculus and also its site of obstruction. Those patients not confirmed to have obstruction by CT are excluded from the study (Figures 1-4).

All data are systematically collected, tabulated, and analyzed using Microsoft Excel and Strata 6 for Windows. Student's *t*-test is used in the univariate analysis for continuous variables, and Chi-square test is used for analysis of non-contiguous data. $P < 0.05$ is considered to be statistically significant.

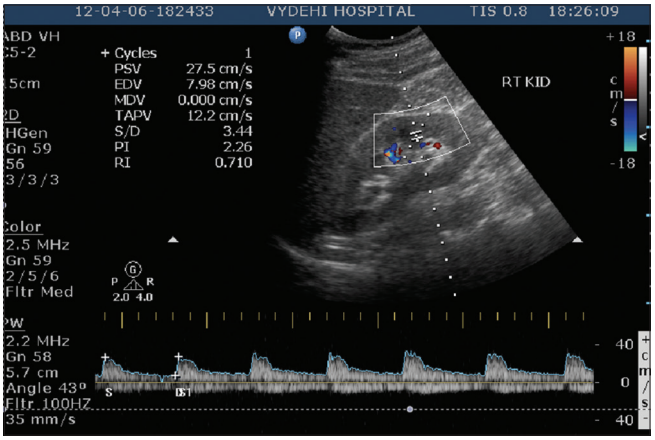


Figure 1: Case 1: Pain since 15 h duration due to right proximal ureteric calculus: Obstructed kidney, resistive indices - 0.71 in interlobar artery

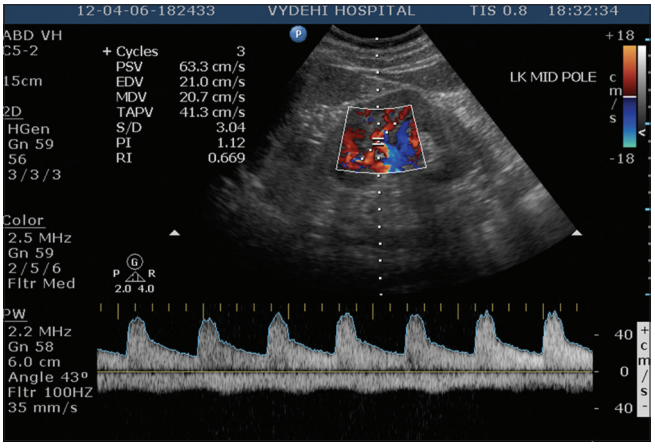


Figure 2: Case 1: Pain since 15 h duration due to right proximal ureteric calculus: Contralateral normal kidney, resistive indices - 0.67 in interlobar artery

RESULTS

In all, 60 patients (120 kidneys; 60 obstructed kidneys as cases and 60 unobstructed contralateral kidneys as controls) were part of this analysis. Doppler is performed in all and subsequently CT scan.

Among 60 patients, 46 were men and 14 were women. The mean age (in years) is 39.24 ± 14.12 (18-65) in men and 34 ± 14.27 (14-55) in women. This difference is statistically not significant (Graph 1).

On gray scale USG, PCS dilatation was observed in 53 (88.4%) patients while it was absent in 7 (11.7%) (Graph 2).

CT confirmed proximal obstruction in 37 cases and distal obstruction in 23 cases (Table 1). In kidneys showing PCS dilatation RI value was 0.7 ± 0.04, in non-dilated kidneys RI value was 0.7 ± 0.06. Arterial Doppler studies were useful in diagnosing acute renal obstruction even in those cases, where PCS dilatation was absent on gray scale USG.

The RI and its mean in obstructed kidneys are significantly higher than in unobstructed kidneys (0.72 vs. 0.63; $P < 0.001$). RI is higher in obstructed kidneys in all the cases. Δ RI, the difference in RI in obstructed (0.05) and unobstructed kidney (0.18) is 0.09 (Table 2).

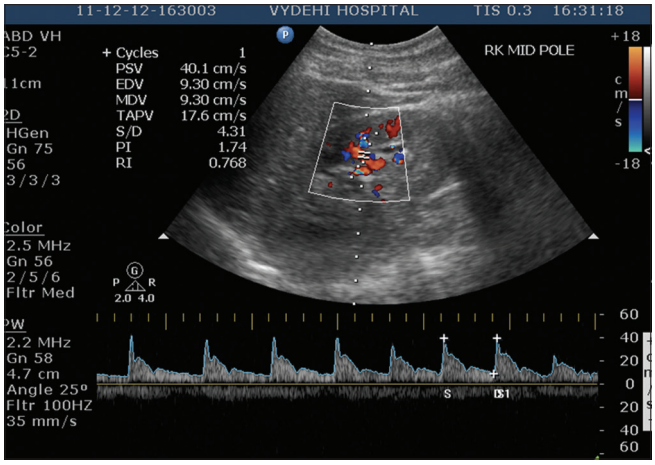


Figure 3: Case 2: Pain since 7 h duration due to right distal ureteric calculus: Obstructed kidney, resistive indices - 0.768 in interlobar artery

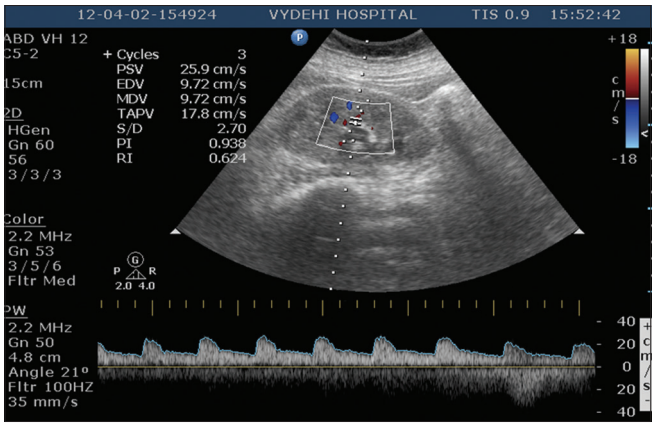


Figure 4: Case 2: Pain since 7 h duration due to right distal ureteric calculus: Contralateral normal kidney, resistive indices - 0.62 in interlobar artery

Table 1: Site of obstruction in CT

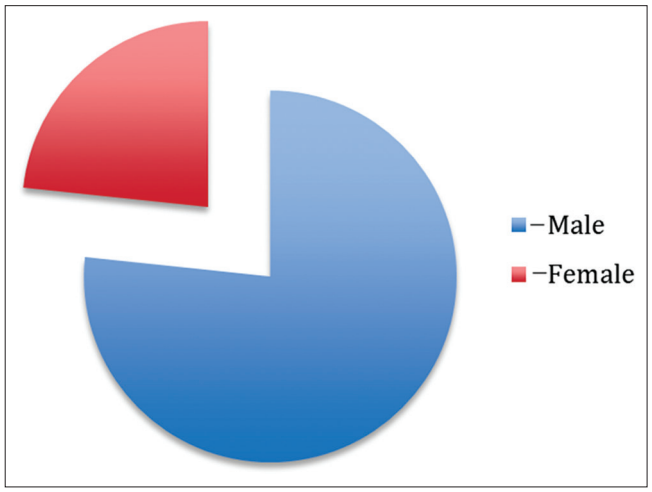
Site of calculus in CT	Frequency
Right proximal	18
Right distal	17
Left proximal	19
Left distal	6

CT: Computed tomography

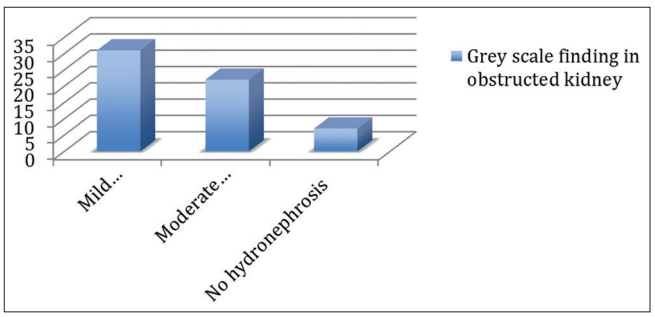
Table 2: RIs in obstructed and unobstructed kidney

Kidney	RI
Obstructed	0.72±0.05
Unobstructed	0.63±0.04
Δ RI	0.09±0.08

RI: Resistive indices



Graph 1: Sex distribution



Graph 2: Gray scale finding in obstructed kidney

The site of obstruction was proximal in 37 (62%) cases and distal in 23 (38%). Mean RI of the obstructed kidneys with distal obstruction was higher (0.72 ± 0.05), than in the kidneys with proximal obstruction (0.70 ± 0.04). However, the difference was statistically not significant ($P = 0.189$).

Most of the patients (48.3%) are evaluated between 6 and 12 h with RI - 0.69, 13.3% within 0-6 h, 21.7% within 13-18 h, and 16.7% within 19-24 h after the onset of symptoms. RI values were similar in the groups evaluated after 6 h (Table 3).

The mean peak systolic velocity in obstructed kidneys was 52.7 ± 13.9 cm/s and in unobstructed kidney was 54 ± 11.4 cm/s. Hence, there were reduced velocities in the peak systolic velocities, and it was statistically significant ($P = 0.042$) (Table 4).

The mean end diastolic velocity in obstructed kidneys was 15.2 ± 5.6 cm/s and in unobstructed kidney was 19.7 ± 3.7 cm/s. Hence, there was reduced end diastolic velocities in obstructed kidney, and it was statistically significant ($P = 0.012$) (Table 5).

DISCUSSION

Gray scale USG is the investigation of choice in the initial evaluation of acute renal obstruction, as it is easily available, portable, and non-ionizing. However, urinary system dilatation seen on gray scale USG is sensitive in 90% but specific in only 65-84% of renal obstruction.[2]

Table 3: Relationship of RI with duration of obstruction

Resistive Indices	0-6 h *N*=8	7-12 h *N*=29	13-18 h *N*=13	19-24 h *N*=10
Obstructed kidney (RI)	0.69±0.07	0.72±0.04	0.71±0.02	0.73±0.04
Unobstructed kidney (RI)	0.62±0.03	0.64±0.03	0.62±0.03	0.61±0.05
Delta (RI)	0.07±0.04	0.07±0.03	0.08±0.05	0.11±0.03

RI: Resistive indices

Table 4: Peak systolic velocity in obstructed and unobstructed kidney

Kidney	Peak systolic velocity cm/s
Obstructed	52.7±13.9
Unobstructed	54±11.4

Table 5: End diastolic velocity in obstructed and unobstructed kidney

Kidney	End diastolic velocity cm/s
Obstructed	15.2±5.6
Unobstructed	19.7±3.7

The sensitivity of USG in detecting PCS dilatation in acute obstruction was 88.3% in our study.

USG is less accurate than excretory urography, as it shows less detail of the PCS anatomy and makes a poor assessment of upper urinary tract drainage. Functional information of the contrast excretion during urography is not provided by USG.[3]

The IVU once the mainstay of diagnosis of acute obstruction is rapidly being replaced by non-contrast enhanced CT.[3] However, CT is expensive.

Acute ureteric obstruction by a calculus results in a complex sequence of changes that is reflected on renal blood flow and ureteric pressure.[6] Whenever there is a unilateral acute ureteric obstruction, in the first 2 h there is will be increase in the renal pelvic pressure due to increasing in renal blood flow due to afferent arteriolar vasodilation.[6] Between 2 and 6 h, there will be reduced blood secondary to renal vasoconstriction. The elevated pelvic pressure seen after 6 h will last for few more hours; after 18 h, the renal blood flow will decrease due to afferent arteriolar vasoconstriction with associated reduction in pelvicalyceal pressure.[7]

The role of renal arterial Doppler USG in the evaluation of acute renal obstruction is vigorously debated.[8] Studies by Rodgers *et al.*[6] and Platt *et al.*[1] have shown an elevated RI in acutely obstructed kidneys, when compared with the RI in normal contralateral kidneys of the same patients. They also found similar results when acutely obstructed kidneys were compared with healthy subjects as control groups.

Tublin *et al.*[3] applied discriminatory thresholds for obstruction (mean RI ≥0.70 and Δ RI ≥0.10) and correlated the results of Doppler solography and found the sensitivity and specificity of Doppler USG were only 44% and 82%, respectively.

In our study of 60 patients, we found that the RI in obstructed kidneys is significantly higher than the RI in the unobstructed kidneys (0.72 vs. 0.63; $P < 0.001$). The RI was higher in obstructed kidneys in all cases. The difference between the obstructed and unobstructed kidneys (Δ RI) ranged from 0.02 to 0.21 with a mean Δ RI of 0.09. Our results correlate well with many studies reported earlier by Badr and Brenner,[9] Shokeir and Abdulmaaboud,[10] Miletic *et al.*[11]

We also investigated the shortest duration of acute renal obstruction that can cause elevation of RI. We divided our patients into four groups (0-6 h, 7-12 h, 13-18 h, and 19-24 h) based on the duration of the renal colic. RI values were similar after 6 h in three groups of patients. But, it was <0.7 in patients presenting between 0 and 6 h

with mean RI of 0.69 ± 0.07 which correlated with the earlier study.[4] This suggests that there is no change in Doppler waveform alterations and takes time for changes to appear and necessitates repeat scan after 6 h of clinical obstruction, this finding is seen in consents with previous studies showing increase in RI occurring after as little as 6 h of clinical obstruction.[12]

We also studied the effect of the level of obstruction on RI values. Distal obstruction had more RI value (0.72 ± 0.05) compared to proximal obstruction (0.7 ± 0.04), and the values were not statistically significant. However, the study done by de Toledo *et al.*[13] showed that patients with proximal ureteric obstruction have RIs higher than those with distal obstruction.

Seven patients who did not have PCS dilatation on USG were later confirmed to have the obstruction on CT. RI values were higher in all these patients (0.71). The sensitivity of USG in detecting PCS dilatation in acute obstruction was 88.3% in our study this is seen in consensus with the recent one done by Saboo *et al.*[14]

CONCLUSION

Gray scale USG is the commonly used modality in the initial evaluation of acute renal obstruction. The sensitivity of gray scale USG for detecting obstruction is found to be 88.3%. Renal arterial Doppler is a useful additional diagnostic tool in diagnosing acute ureteric obstruction even when the PCS is not dilated. The site of obstruction affected the RI values in which distal obstruction had a higher value than proximal obstruction. The duration of symptoms at presentation affected the RI values in acute ureteric obstruction and was positive in only after 6 h necessitating repeat Doppler study after first 6 h of renal colic.

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Original Article

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Role of Liver Function Tests and Serum Lactate Levels in Predicting the Severity of Acute Paraquat Poisoning

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Abstract

Introduction: The paraquat is a liquid herbicide associated with both accidental and intentional ingestion, leading to severe and often fatal toxicity.

Aim: The present study is to evaluate the role of liver function tests and lactate levels in predicting the outcome of acute paraquat poisoning.

Materials and Methods: A total of 30 patients with acute paraquat poisoning admitted in intensive care unit (ICU) were included in the study. The paraquat poisoning was confirmed by urine dithionite test. Initial clinical parameters such as vital signs, age, amount of paraquat consumption, respiratory rate, serum creatinine, bilirubin, alanine transaminase (ALT), aspartate transaminase (AST), and lactate levels were obtained at the time of admission to ICU. Depending on the outcome after paraquat poisoning the patients were categorized as survivors and non-survivors, the trend in the clinical parameters was assessed to observe the severity.

Results: The overall mortality rate was 66.6% (20/30) during 3 days follow-up, on the 1st day of admission serum bilirubin, AST, ALT, and lactate levels were statistically significantly high in non-survivors when compared with survivors.

Conclusion: The 1st day of admission serum bilirubin, AST, ALT, and lactate levels are very much elevated and are useful in predicting the outcome of paraquat poisoning.

Key words: Acute paraquat poisoning, Predictors, Outcome, Survivors

INTRODUCTION

Paraquat also known as gramoxone is an organic nitrogen heterocyclic herbicide used in agriculture throughout the world. Its active component is the 1, 1'dimethyl-4, 4'dipyridine cationic compound.[1,2] It is highly toxic to the humans; intentional or accidental ingestion of paraquat is frequently fatal due to the failure of multiple organs.[3] An estimated of 250,000 to 370,000 people die all over the world from pesticide poisoning each year, and around 90% of the patients with paraquat poisoning had taken concentrate paraquat in liquid form orally.[4] Many critical care practitioners tried different therapeutic modalities for the management of acute paraquat poisoning cases, but still high mortality rate is see.[5] Hence, reliable predictors are required for assessing the severity of acute poisoning, which help in framing proper treatment plans to have a better outcome. So far, several markers have been reported to assess the severity including plasma paraquat concentration, Apache II, SOFA score, and estimated ingestion dose of paraquat;[6] out of these, the best marker is plasma paraquat concentration, but the estimation of plasma paraquat concentration is more complicated process which requires expensive equipment and good quality controls.[7]

Therefore, alternative clinical markers which are cheaper and possess' good quality controls are required to predict

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the severity of acute paraquat poisoning. The aim of the present study is to evaluate the importance of less expensive serum bilirubin, aspartate transaminase (AST), alanine transaminase (ALT), and lactate levels on the 1st day of admission in intensive care unit (ICU) for predicting the severity of acute paraquat poisoning.

MATERIALS AND METHODS

The present study was approved by the institutional ethics committee of NRI Medical College and Hospital. This is a prospective study of patients with acute paraquat poisoning admitted to ICU from January 2011 to January 2015. A total number of 30 patients included in the study, who met with the following criteria: (1) Patients had a history of attempted suicide through paraquat ingestion with circumstantial evidence such as empty paraquat container, (2) patients who tested positive in urine dithionite test for acute paraquat poisoning and displayed typical clinical features such as vomiting, oral ulcers, and difficulty in swallowing. Patients were excluded if they had chronic liver disease, chronic kidney disease, diabetes, and drunken alcohol before the ingestion of paraquat. All the patients were given standard treatment protocol. Initial biochemical parameters such as serum creatinine, bilirubin, ALT, AST, and lactate levels were analyzed at the time of admission to ICU i.e., on the 1st day of admission by collecting 5 ml of blood sample from all the patients using Dade dimensions auto analyzer after standardizing the above said parameters using Bio-Rad quality controls. The same parameters were measured on the 2nd and the 3rd day also. The patients were categorized as survivors and non-survivors depending on whether they survived after a follow-up of 3 days; the trend in the biochemical parameters were assessed to observe the severity. The data were presented as a mean ± standard deviation for continuous variables and frequency in percentage for a categorical variable. A $P < 0.05$ was considered a statistically significant.

RESULTS

A total number of 30 patients with acute paraquat poisoning who were admitted to ICU from January 2011 to January 2015 were included in the study. Of 30 patients, the survivors were 33.3% and non-survivors 66.6%, the mean serum creatinine in survivors was 1.3 mg/dl ± 1.6 and in non-survivors was 2.3 mg/dl ± 2.1 with a $P < 0.005$. The mean serum total bilirubin in survivors was 0.9 mg/dl ± 0.16 and in non-survivors was 3.1 mg/dl ± 1.19 with a $P < 0.005$. The mean serum ALT in survivors was 34.4 IU/L ± 60.1 and in non-survivors was 64.5 IU/L ± 110.6 with a $P < 0.005$. The mean serum AST in survivors was 38.2 IU/L ± 66.5 and in non-survivors were 69.4 IU/L ± 120.8 with a $P < 0.005$. The mean serum lactate in survivors was 26.1 mg/dl ± 10.8 and in non-survivors was 72.7 mg/dl ± 20.2 with a $P < 0.005$ (Table 1).

Graph: 1 shows significant rise of Serum bilirubin levels in non survivors when compared to survivors. Graph: 2 shows significant rise of Serum alanine transaminase levels in non survivors when compared to survivors. Graph: 3 shows significant rise of Serum aspartate transaminase levels in non survivors when compared to survivors. Graph: 4 shows significant rise of Serum lactate levels in non survivors when compared to survivors.

It is observed that the mean serum lactate levels were significantly increased from the 1st day to the next 2 days in non-survivors, whereas in survivors the mean serum lactate levels were significantly decreased. (Graphs 5 and 6)

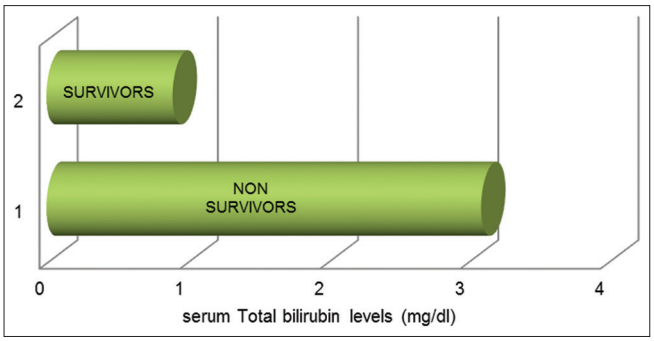
DISCUSSION

The aim of this study was to identify the reliable predictors to assess the severity of paraquat poisoning. Paraquat poisoning is a significant cause of death around the world.[8] The severity of paraquat poisoning may depend on the amount of the paraquat exposure, absorption, and vulnerability of an individual. Many studies revealed various predictors which assess the severity of paraquat poisoning.[9-11] Our study revealed a new relation between initial clinical parameters such as total bilirubin, AST, ALT, and lactate levels on admission and survival of the patient. The toxicity of paraquat is through redox cycling, leading to generation of superoxide anions. These may react to form hydrogen peroxide and subsequently the highly reactive hydroxyl radical, which is thought to be responsible for lipid peroxidation and cell death.[12] Systemic effects of paraquat poisoning are renal and hepatic failure, pulmonary edema and fibrosis, cardiac failure, shock, convulsions, and multi-organ failure. In our study, serum total bilirubin, AST, and ALT were elevated very much in non-survivors compared to survivors shows that liver is affected immediately after paraquat ingestion which highlight the importance of LFT in acute paraquat poisoning which go in accordance with

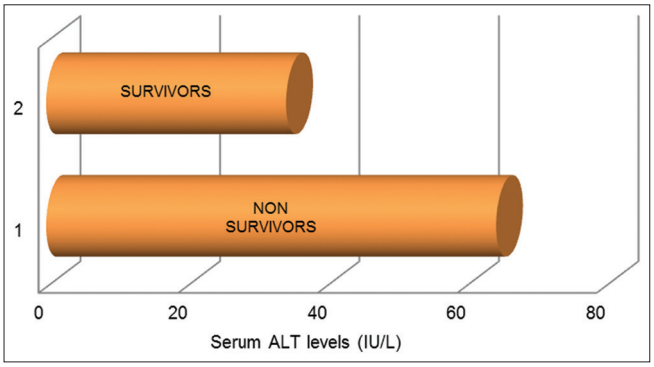
Table 1: Comparison of initial parameters of 30 paraquat poisoning cases on the 1st day of admission between non-survivors and survivors

Parameters	Non-survivors (*n*=20)	Survivors (*n*=10)	*P* value
Creatinine (mg/dl)	2.3±2.1	1.3±1.6	<0.005
Total bilirubin (mg/dl)	3.1±1.19	0.9±0.16	<0.005
ALT (IU/L)	64.5±110.6	34.4±60.1	<0.005
AST (IU/L)	69.4±120.8	38.2±66.5	<0.005
Lactate levels	72.7±20.2	26.1±10.8	<0.005

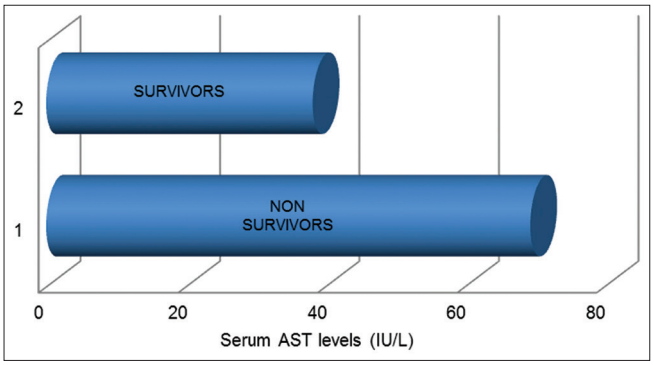
ALT: Alanine transaminase, AST: Aspartate transaminase



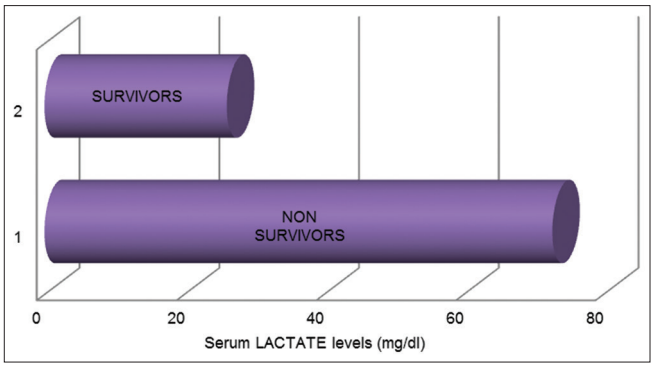
Graph 1: The mean initial serum total bilirubin levels in non-survivors were significantly higher than survivors



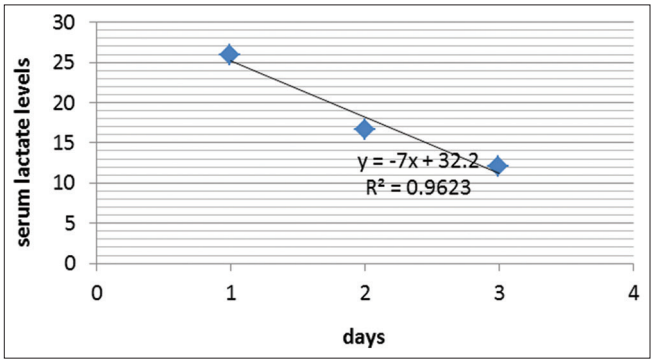
Graph 2: The mean initial serum alanine transaminase levels in non-survivors were significantly higher than survivors



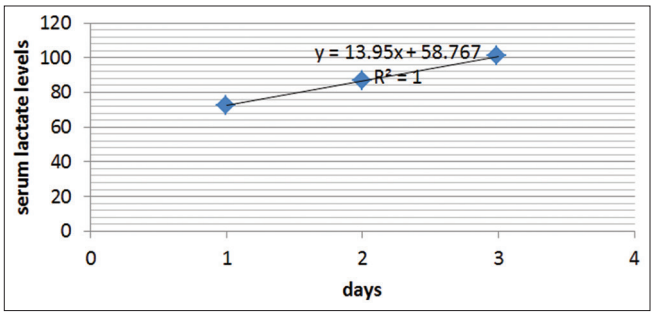
Graph 3: The mean initial serum aspartate transaminase levels in non-survivors were significantly higher than survivors



Graph 4: The mean initial serum lactate levels in non-survivors were significantly higher than survivors



Graph 5: The rate of decrease in the mean serum lactate levels on the 1st, 2nd, and 3rd day in survivors



Graph 6: The rate of increase in the mean serum lactate levels on the 1st, 2nd, and 3rd day in non-survivors

other studies stating that substantial proportion of paraquat patients suffered from hepatic complications[13] and liver may show pallor, mottled appearance and fatty changes due to microscopic centrilobular necrosis.[14] In our study, serum lactate levels at the time of admission were elevated very much in non-survivors when compared to survivors which shows the anoxic conditions of various tissues, highlights the importance of serum lactate levels in predicting the severity of acute paraquat poisoning, which in accordance with other researchers stating that initial lactate levels were higher in non-survivors than in survivors.[15] It was also observed that the other initial clinical parameters such as blood pH, respiratory rate, and serum creatinine were associated with the survival after acute paraquat poisoning.

CONCLUSION

Paraquat consumption is a common agent of suicidal poisoning in this part of India, resulting in very high mortality. As there is no specific antidote for paraquat poisoning, the mainstay of treatment is supportive. In this situation, predictors for severity of acute paraquat poisoning play a major role in determining the prognosis. Our results suggest that initial clinical parameters such as serum total bilirubin, AST, ALT, and lactate levels are very

good predictors to assess the outcome of acute paraquat poisoning.

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Original Article

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Liver Function Abnormalities in Human Immunodeficiency Virus Positive Individuals and its Correlation with Disease Severity

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Abstract

Background: Human immunodeficiency virus (HIV) infection is characterized by an irreversible and profound immunosuppression. Liver enzyme elevations are common in HIV-infected patients, and highly active antiretroviral therapy (HAART) has completely modified the pattern of hepatic events in HIV-infection. The early recognition and diagnosis of hepatic events will be useful in the safe and effective use of HAART and enhance the survival of HIV-infected patients.

Objectives: The present study was done to identify various liver function abnormalities in HIV-positive patients and its correlation with CD4 count.

Materials and Methods: The study included 100 HIV positive patients selected from Sri Ramachandra Medical College and Hospital from the year 2012 to 2014. Complete hemogram, blood urea, serum creatinine, liver function tests (LFTs), CD4 count, hepatitis B surface antigen, anti-hepatitis C virus, and ultrasound abdomen were done for all the patients. The study population was divided into three groups based on CD4 count. Group I included 50 patients with CD4 count <200 cells per cu.mm, 28 patients in Group II with CD4 count between 201 and 350, and Group III included 22 patients with CD4 count more than 350. About 39 patients were on ART and 34 patients were on antituberculous treatment.

Results: 63 patients had an abnormal LFT, out of which 29 patients had the hepatocellular injury, 6 patients had a cholestatic liver injury, and 28 patients had a mixed pattern of liver injury. Ultrasound abdomen revealed fatty liver in 24 patients, hepatomegaly in 8 patients, hepatosplenomegaly in 6 patients, cirrhosis of the liver in 5 patients, splenomegaly in 3 patients, ascites in 3 patients, ileocecal tuberculosis in 2 patients, and hepatocellular carcinoma in 1 patient.

Conclusion: HIV-infected patients are at a higher risk of the liver function abnormalities. The incidence of liver function abnormality increases with severity of the disease.

Key words: CD4 count, Highly active antiretroviral therapy, Human immunodeficiency virus infection, Liver function

INTRODUCTION

Liver enzyme elevations are common in human immunodeficiency virus (HIV) infected patients. The complex pathogenic mechanisms of liver injury make their diagnosis and management difficult. These include hepatotoxicity related to the highly active antiretroviral therapy (HAART) regimen, idiosyncratic or immunoallergic mechanisms, and direct cytotoxicity enhanced by an underlying liver disease. Co-infection with hepatitis B virus (HBV) or hepatitis C virus (HCV) infection can also worsen liver function either due to direct cytotoxicity or other immune mechanisms involved. In addition to the above alcohol-related liver disease, non-alcoholic steatohepatitis associated with metabolic syndromes (e.g., hyperlipidemia, diabetes, or being overweight) and use of medication or illicit drugs (e.g., methamphetamine) can further contribute to the deterioration of liver function.

At the beginning of HIV era, liver dysfunction mainly corresponded with opportunistic infections (e.g., with

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cytomegalovirus [CMV] or mycobacteria and leishmaniasis), including AIDS-related cholangitis associated with parasitic infections (cryptosporidiosis and microsporidiosis), viral infections (e.g. with CMV), or mycobacterial infections; tumors (lymphoma and Kaposi sarcoma); and drug-related hepatitis (caused by trimethoprim-sulfamethoxazole and other antibiotics). All of these reflected a worse prognosis. The development of HAART (regimens composed of nucleoside reverse-transcriptase inhibitors [NRTIs], protease inhibitors [PIs], and non-NRTIs [NNRTIs]) has resulted in a significant decrease in morbidity and mortality among HIV-infected patients.[1] HAART has modified the pattern of hepatic events in HIV-infection, and the liver should be an important consideration when treating HIV-infected patients.[2]

Pathogenesis of liver fibrosis could be explained by direct effect on hepatocytes, hepatic stellate cells (HSCs), and Kupffer cells (KCs). In the absence of productive infection, gp120 binding to CXCR4 may induce hepatocyte apoptosis and activation of HSCs. NRTIs and HIV itself (via peroxisome proliferator-activated receptor effects) may also contribute to liver disease by inducing the metabolic syndrome. An increase in lipopolysaccharide (LPS) in HIV can stimulate hepatocytes, KCs, and HSCs to produce pro-inflammatory cytokines and chemokines (tumor necrosis-α, transforming growth factor-β and interleukin) which attract activated lymphocytes and monocytes to the liver and further drive fibrosis.

Various studies demonstrate HIV-infection of hepatic cells. KCs can be infected by HIV *in vivo*.[3] *In vitro* studies suggest that HIV-infection of KCs leads to productive infection.[4-7] HIV can also induce hepatocyte apoptosis *in vitro* via gp120 signaling through CXCR4 in the absence of infection.[8] HIV-infection of GI tract associated CD4+ T-cells leads to increased permeability to bacterial endotoxins such as LPS. Elevated LPS has been shown to contribute to liver disease progression in alcoholic liver disease[9,10] as well as in non-alcoholic fatty liver disease and non-alcoholic steatohepatitis.[11-13] In addition to activation of KCs, LPS also directly activates HSC to produce CCL-2,[14] and *in vitro* following co-culture with monocytes, induces hepatocytes to produce chemokines CXCL9, 10 and 11.[15] These chemokines will induce chemotaxis of both T-cells and monocytes to the liver.

Hepatotoxicity due to ART may be related to agents from some classes, including NRTIs, NNRTIs, and PIs. The severity of hepatotoxicity may range from transient elevations in transaminase levels to hepatic failure and death, via a variety of mechanisms. NNRTI such as nevirapine and efavirenz may cause hypersensitivity. NRTI, primarily didanosine, may cause direct mitochondrial toxicity leading to abnormal liver function. Other mechanisms by which ART causes liver-related toxicity include direct cell stress and disturbances in lipid/sugar metabolism and steatosis, as seen with PIs. Ritonavir, tipranavir, and darunavir have all been associated with elevations in ALT.

The present study was done to observe the pattern of abnormal liver function tests (LFTs) in HIV-positive patients and its correlation with CD4 count.

MATERIALS AND METHODS

This study was a cross-sectional study of 100 HIV-positive patients conducted at Sri Ramachandra Medical College in the Department of Medicine from July 2012 to August 2014 after approval of Hospital Ethics Committee. All patients fulfilling inclusion criteria (all HIV-seropositive patients, seropositivity being confirmed by ELISA) were screened and investigations done. Patients with age <18 years and pregnant patients were excluded from the study.

A questionnaire for detailed history was taken from all patients and a thorough physical examination was done. Abdomen examination was done to demonstrate hepatomegaly, splenomegaly, free fluid or cirrhosis of the liver. Complete blood count, blood urea, sugar, serum creatinine, LFTs including coagulation profile, hepatitis B surface antigen (HBsAg), anti-HCV, and urine analysis were done for all patients. The CD4 lymphocyte count was done by flow cytometry method. Abnormal LFTs were defined as >1.25 ULN in HIV-positive patients.

The collected data were analyzed using Statistical Package of Social Sciences 17.0 for Windows. Data were expressed as the mean ± standard deviation. A $P < 0.05$ was considered statistically significant.

RESULTS

The majority of the patients in the study were aged between 31 and 50 years (73%). 65 patients were males, and 35 patients were females (mean age was 40.91 years). Fever was the most common symptom (63 patients) followed by abdominal pain (22 patients). Pallor was the most common general examination finding (34 patients) followed by pedal edema (6 patients), icterus (5 patients), clubbing (3 patients), and generalized lymphadenopathy (3 patients). About 19 patients were positive for HBsAg, 3 patients were positive for the anti-HCV antibody.

The study population was divided into three groups based on CD4 count. Group I included 50 patients with a CD4

count <200 cells per cu.mm, 28 patients in Group II with a CD4 count between 201 and 350, and Group III included 22 patients with a CD4 count more than 350. 39 patients were on ART and 34 patients were on antituberculous (TB) treatment. The most common opportunistic infection was oral candidiasis (22 patients), pulmonary TB in 19 patients and esophageal candidiasis in 9 patients. 39 patients were receiving HAART. 39 patients (100%) were on NRTI, 34 patients (87.17%) were on NNRTI, 5 patients (12.8%) were on PI. 29 patients were on efavirenz, 28 were on tenofovir, 20 were on lamivudine, 18 were on zidovudine, and 5 patients were on atazanavir therapy.

Normal ultrasound was found in 43 patients. Fatty liver was the most common ultrasound finding (24 patients), hepatomegaly in 8, splenomegaly in 3, and hepatosplenomegaly in 6 patients.

There was a statistically significant correlation for the CD4 count with serum glutamate oxaloacetate transaminase (SGOT), serum glutamic pyruvate transaminase (SGPT), alkaline phosphatase, and international normalized ratio (INR) abnormality. SGOT, SGPT, alkaline phosphatase, and INR values were more abnormal in the group of patients with a CD4 count <200 cells per cu.mm. There was no statistically significant correlation between, ART, anti-tubercular treatment (ATT), alcohol use, and LFT abnormality in our study.

DISCUSSION

In our study, the mean age of study population was 40.91 years. In the study done by Ejilemele *et al.*,[15] the mean age was 35.6 years. In the study done by Sterling *et al.*,[16] the mean age was 42 years.

63% patients had abnormal LFT. Out of which 29 patients (46%) were classified as hepatocellular injury, six patients (9.5%) had a cholestatic liver injury and 28 patients (44.5%) had mixed pattern. In the study by Ejilemele *et al.*, out of 129 patients, 113 patients (87.6%) had LFT abnormality. Out of which 94 patients (85.5%) had hepatocellular injury, 16 patients (14.5%) had a cholestatic liver injury. In the study by Ocama *et al.*, 8% patients had a hepatocellular injury, 63% patients had the cholestatic pattern and 19% patients had a mixed pattern of injury. Thus, our study results were similar to the study by Ejilemele *et al.*, where the most common LFT abnormality was hepatocellular injury.

Elevated SGOT, SGPT, ALP was observed in 67%, 60%, and 36% of patients, respectively. In the study done by Sterling *et al.*, elevated SGOT, SGPT, and ALP were observed in 31.5%, 23.8%, and 46.9% of patients, respectively. In relation to CD4 count, 40 patients had elevated SGOT in the Group I, 18 patients had elevated SGOT in the Group II and nine patients in the Group III with a *P* value of 0.005 which is statistically significant. 38 patients had elevated SGPT in the Group I, 17 patients

Table 1: CD4 count and total bilirubin

CD4 count	Total bilirubin<1.5 (%)	Total bilirubin>1.5 (%)	Total
<200	44 (50)	6 (50)	50
201-350	25 (28.4)	3 (25)	28
>350	19 (21.6)	3 (25)	22
Total	88	12	100

P=0.951

Table 2: CD4 count and SGOT

CD4 count	SGOT<44 (%)	SGOT>44 (%)	Total
<200	10 (30.3)	40 (59.7)	50
201-350	10 (30.3)	18 (26.9)	28
>350	13 (39.4)	9 (13.4)	22
Total	33	67	100

P=0.005. SGOT: Serum glutamate oxaloacetate transaminase

Table 3: CD4 count and SGPT

CD4 count	SGPT<51	SGPT>51	Total
<200	12 (30)	38 (63.3)	50
201-350	11 (27.5)	17 (28.3)	28
>350	17 (42.5)	5 (8.3)	22
Total	40	60	100

P<0.001. SGPT: Serum glutamic pyruvate transaminase

Table 4: CD4 count and ALP

CD4 count	ALP<161 (%)	ALP>161 (%)	Total
<200	22 (34.4)	28 (77.8)	50
201-350	22 (34.4)	6 (16.7)	28
>350	20 (31.2)	2 (5.6)	22
Total	64	36	100

P<0.001. ALP: Alkaline phosphatase

Table 5: CD4 count and INR

CD4 count	INR<1.1 (%)	INR>1.1 (%)	Total
<200	39 (60)	11 (31.4)	50
201-350	13 (20)	15 (42.9)	28
>350	13 (20)	9 (25.7)	22
Total	65	35	100

P=0.016. INR: International normalized ratio

Table 6: CD4 count and albumin

CD4 count	Albumin<3.2 (%)	Albumin>3.2 (%)	Total
<200	30 (49.2)	20 (51.3)	50
201-350	16 (26.2)	12 (30.8)	28
>350	15 (24.6)	7 (17.9)	22
Total	61	39	100

P=0.714

had elevated SGPT in the Group II and five patients in the Group III with a $P < 0.001$ which is statistically significant. 28 patients had elevated ALP in the Group I, 6 patients had elevated ALP in the Group II and 2 patients in the Group III with a $P < 0.001$ which is statistically significant. Hence, there was significant correlation between CD4 count and LFT abnormality. LFT abnormalities are inversely proportional to CD4 count. This finding correlated well with Sterling *et al.* study.

Correlation between anti-TB therapy and LFT abnormality was not statistically significant in our study. In the study by Ponsiano *et al.*, use of isoniazid was the common cause of hepatotoxicity. Anti-TB drugs induced liver injury is the most common cause drug-induced liver injury, but in our study, there was no statistically significant relationship between ATT and LFT abnormality. This may be because the group of patients not on ATT had LFT abnormality due to other causes like use of ART, low CD4 count, direct effect of HIV and co-infections.

Limitations of the Study

This is not a case-control study, where the study population is not compared with control group (normal individuals). The most important limitation of our study was a lack of histology. Hence, the clinical significance of mild liver enzyme elevations could not be assessed. Our study population was very less, which does not reflect the entire scenario of HIV-infected individuals. Hence, further study with a larger study population and liver histology is recommended in our country.

CONCLUSION

HIV-infected patients are at higher risk of liver function abnormalities. The incidence of liver function abnormality increases with severity of disease. It is, therefore, important to characterize the nature of liver dysfunction to institute appropriate management.

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Original Article

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Demographic, Clinical Profile of Oral Lichen Planus and its Possible Correlation with Thyroid Disorders: A Case-Control Study

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Abstract

Objectives: Oral lichen planus (OLP) is one of the common chronic conditions involving the oral mucosa. It is more common and persistent than the cutaneous form causing significant discomfort to the patient. The aim is to study the demographic pattern, clinical profile, and to find out any possible correlation with the thyroid disorders.

Materials and Methods: A total of 50 patients comprising 32 females and 18 males of OLP, and an equal number of age and sex-matched controls were evaluated, for demographic trends, clinical profiling, and relevance to thyroid disorders.

Results: Out of 50 OLP patients the thyroid function tests (TFTs) were deranged in 9 (18%); 5 females and 4 males while in the control group, TFTs were deranged in 1 (2%) female. The results obtained were statistically significant ($P < 0.05$).

Conclusions: The results of our study show that a significant percentage of OLP patients have deranged thyroid function, especially hypothyroidism. As the sample size in our study was small, this calls for further studies involving a larger number of patients.

Key words: Demographic, Diagnosis, Etiology, Lichen planus, Oral mucosa, Thyroid

INTRODUCTION

Oral lichen planus (OLP) is a mucocutaneous disease which can affect the skin, oral mucosa, and other mucous membranes. The etiology of LP which is an inflammatory mucocutaneous disease is unknown and thought to arise as a result of an immune response – mainly by CD8+ lymphocytes – to antigens on lesional keratinocytes.[1,2] English physician Erasmus Wilson in 1866 presented the designation and description of the pathology. He also suggested "nervous tension" could be the cause of its etiology.[3] It was Louis-Frédéric Wickham who provided an addition to the description of the lesion stories et punctuations grisatre (grayish striae and dots), named Wickham Striae in 1895.[4]

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The clinical course of OLP lesions normally last for years with alternating periods of exacerbation and quiescence. There is an increase in pain and erythematous or ulcerated areas and during the exacerbation phase.[5] This phase is also associated with periods of anxiety, psychological stress, and mechanical trauma (Koebner phenomenon). Chronic low-intensity irritation due to the presence of plaque or dental calculus may also increase the severity of gingival LP and is considered Koebner phenomenon, other factors such as the mechanical trauma of odontological procedures, friction of sharp points, rough dental restorations, heat and cigarette irritants, and oral habits like chewing gum.[6,7]

The clinical presentation of OLP ranges from mild, painless white keratotic lesions to painful erosions and ulcerations.[8] The most common affected site is buccal mucosa, usually bilateral. Clinically OLP may occur in six clinical variants as reticular, papular, plaque-like, erosive, atrophic, and bullous as classified by Andreasen.[9]

The reticular variant of OLP is the most recognized form, encompass white lesions, which clinically appear as a

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network of connecting and overlapping lines, papules or plaques. Although clinical presentation in certain patients may be an impressive array of diffuse and widespread reticulated lesions, they are usually asymptomatic and often, are unaware of the presence of these lesions. A significant degree of discomfort is associated with the erythematous and erosive OLP lesions. The site, size and a number of ulcerations is variable; rarely, bulla may be observed in the erosive form as they rupture easily.[10] In the case of erosive lesions, the remission is not spontaneous and as such due to the similarity in clinical features it may lead to confusion with other autoimmune mucosal, vesiculo-erosive diseases. The most frequent intraoral site of involvement is the posterior part of buccal mucosa followed by the tongue, gingiva, labial mucosa, and vermilion of the lower lip.[7,11,12] It has been observed that OLP affects from 0.1 to about 4% of individuals, occurring mostly in middle-aged adults, with a female predominance at a ratio of approximately 2:1.[13,14] It has been found that, approximately, 15% of the patients with OLP develop cutaneous lesions and genital lesions have been found in exist in 20% of the patients diagnosed with OLP.[15,16] One of the most important complications concerning the progression and prognosis of OLP is the development of oral squamous cell carcinoma with a frequency of malignant transformation 0.4-5.3%[17] which led the World Health Organization (WHO) to classify OLP as a potentially malignant disorder.[18]

MATERIALS AND METHODS

In the present study 50 patients diagnosed with OLP who visited the Department of Oral Medicine and Radiology, were selected and an equal number of age and sex-matched controls were enrolled in the study. The diagnosis of OLP was made as per the criteria's specified by the WHO as follows:

WHO Clinical Definition of OLP[19]

Clinical criteria:

1. Presence of bilateral lesions
2. Presence of a network of a slightly raised grayish white striae (reticular form)
3. Erosive, atrophic, bullous or plaque-like lesions (accepted as subtypes only in the presence of reticular lesions in some part of oral mucosa).

A detailed medical history was recorded for all the patients followed by a thorough clinical examination. Thyroid function was assessed using triiodothyronine (T3), and thyroxine (T4), thyroid-stimulating hormone (TSH) levels recorded by radioimmunoassays for both the groups. The age and sex distribution pattern of these patients were recorded, and they were divided into five groups based on the age. Intraoral distribution of the lesions according to clinical variants-(reticular, erosive and atrophic) and based on the site involved (buccal mucosa, gingiva, labial mucosa, tongue, palate, and floor of mouth) was recorded. Patients selected for the present study were in the age group of 20-70 years.

Statistical Methods

Statistical software Statistical Package for the Social Sciences (Version 20.0) by IBM was used to carry out the statistical analysis of data. Data were analyzed using descriptive statistics *viz.*, percentages, means, and standard deviations. Student's independent *t*-test was employed for parametric data. Chi-square test or Fisher's exact test whichever appropriate was applied for non-parametric data. A $P < 0.05$ was considered statistically significant.

RESULTS

In the present study 50 patients diagnosed with OLP who visited the Department of Oral Medicine and Radiology, were selected along with 50 age and sex matched controls. These patients comprised 18 male patients in the OLP group and 32 female patients and an equal number of patients for each gender and age were selected for the control group (Table 1) & (Graph 1).

These lesions comprised typical reticular form, erosive as well as atrophic form. The reticular type was the most common form present in 37 patients, followed by erosive in 11 patients and atrophic in 2 patients in the OLP group. The reticular form was present in 14 out of 18 male patients, and 23 out of 32 female patients, whereas erosive form was present in 04 male patients and 07 female patients, and atrophic form was only present in 02 female patient (Table 2) & (Graph 2).

Table 1: Age and gender distribution of patients

Age (years)	*n* (%)			*P* value
	Male (*n*=18)	Female (*n*=32)	Total	
20-30	4 (22.2)	5 (15.6)	9 (18)	0.115#
31-40	6 (33.3)	6 (18.8)	12 (24)	
41-50	5 (27.8)	9 (28.1)	14 (28)	
51-60	2 (11.1)	7 (21.9)	9 (18)	
61-70	1 (5.6)	5 (15.6)	6 (12)	
Mean±SD	39.1±11.86	45.2±13.19	43.0±12.94	

#Statistically non-significant difference ($P<0.05$), SD: Standard deviation

Table 2: Distribution of OLP lesions according to clinical variant

Clinical variant	Male	Female	Total (*n* (%))
Reticular	14	23	37 (74)
Erosive	4	7	11 (22)
Atrophic	0	2	2 (4)

OLP: Oral lichen planus

Multiple oral lesions were also present at different sites in the oral cavity (Figure 1), with buccal mucosa being predominantly in the picture in most of the cases followed by gingiva and tongue. Isolated lesions involving palate, the floor of mouth were also present (Table 3) & (Graph 3).

In the OLP group, the thyroid function tests (TFT's) were found deranged in 9 (18%) patients; five females and four males (Table 4a) & (Graph 4).

In the control group, TFT's were deranged in only one female patient only (2%), suggestive of hypothyroidism (T3↓, T4↓, TSH↑) (Table 4b) (Graph 4).

On drawing the comparison of an outcome of thyroid function in two groups (OLP group and control group).

Table 3: Intra oral distribution of OLP lesions according to site

Site	Number of patients	Percentage
Buccal mucosa	44	88
Gingiva	16	32
Labial mucosa	8	16
Tongue	9	18
Palate	7	14
Floor of mouth	9	18

OLP: Oral lichen planus

Table 4a: Patients with altered thyroid profile with OLP

Age	Sex	Clinical presentation	Thyroid profile
43	F	Reticular	T3↓ T4↓ TSH↑
27	M	Reticular/erosive	T3↓ T4↓ TSH↑
45	F	Atrophic	T3↓ T4↓ TSH↑
39	F	Reticular/erosive	T3↓ T4↓ TSH↑
38	F	Erosive	T3↓ T4↓ TSH↑
47	M	Reticular/erosive	T3↓ T4↓ TSH↑
43	F	Reticular/erosive	T3↓ T4↓ TSH↑
49	M	Reticular/erosive	T3↓ T4↓ TSH↑
57	M	Reticular/erosive	T3↓ T4↓ TSH↑

OLP: Oral lichen planus

Table 4b: Patients with altered thyroid profile in control group

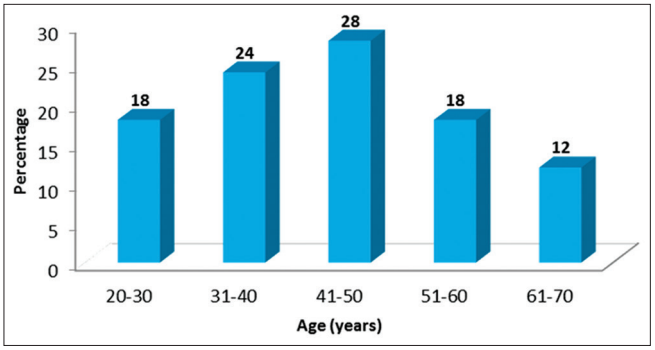
Age	Sex	Clinical presentation	Thyroid profile
43	F	No clinical features suggestive of OLP	T3↓ T4↓ TSH↑

TSH: Thyroid-stimulating hormone, OLP: Oral lichen planus

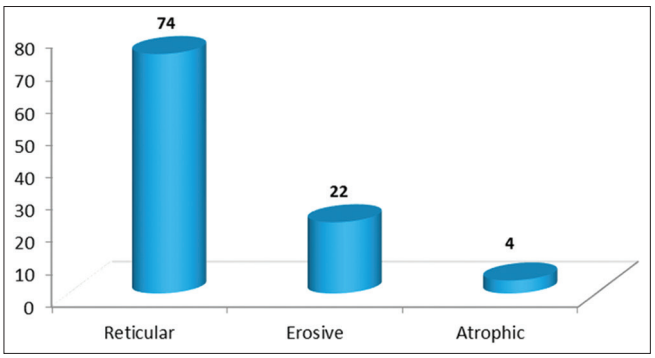
Table 5: Comparison of outcome of thyroid function in two groups

TFT	*n* (%) (*n*=50)		*P* value
	OLP group	Control group	
Abnormal	9 (18)	1 (2)	0.016*
Normal	41 (82)	49 (98)	

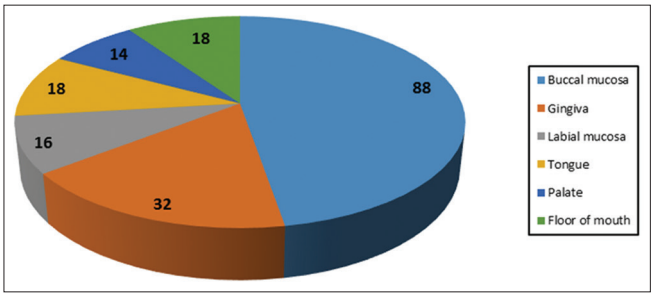
*Statistically significant difference (*P*<0.05). OLP: Oral lichen planus, TFT: Thyroid function tests



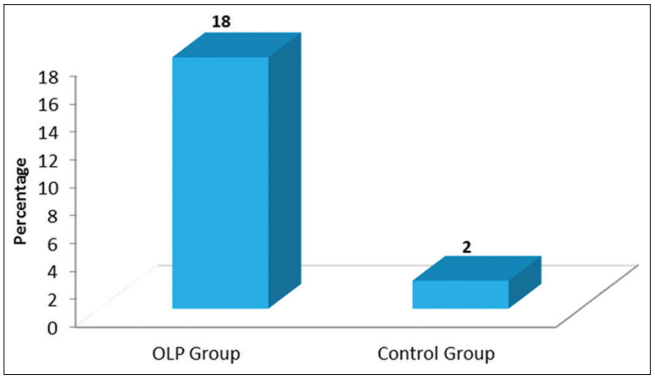
Graph 1: Age distribution of studied patients



Graph 2: Intraoral distribution of oral lichen planus lesions according to clinical variant



Graph 3: Distribution of oral lichen planus lesions according to site



Graph 4: Abnormal thyroid function in patients among two groups

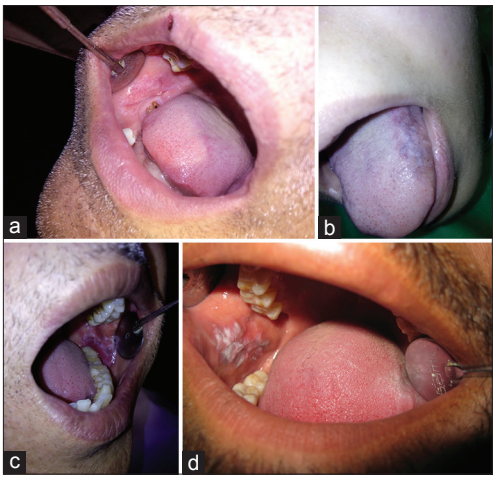


Figure 1: (a-d) Clinical presentation of oral lichen planus

Statistically significant difference was obtained with the $P < 0.05$ (Table 5).

DISCUSSION

LP is a relatively common disorder, estimated to affect 0.5-2.0% of the general population.[20] Apart from being more common than the cutaneous form, OLP tends to be more persistent and more resistant to treatment.[21]

In the present study, demographic pattern, clinical profile of OLP patients was recorded, and an effort was made to find out any possible correlation with the thyroid disorders among the patients diagnosed for OLP, who visited the Department of Oral Medicine and Radiology. The data obtained from the present study is in coherence with the data of other similar studies with respect to clinical presentation, symptoms reported by the patients, duration of the disease and medical history. Further, it was observed that the occurrence of OLP is more common in females than males, which is in accordance with most of the studies conducted in the past.[22] LP affects primarily middle-aged adults, and the prevalence is a greater than women. In our study, the prevalence of OLP was seen in the 4th decade of life which is slightly lower than the age group reported in various studies and slightly more than some of the reported studies.[12,23] The intraoral lesions were typically bilateral, symmetrical, and the buccal mucosa was the most common site of involvement followed by gingiva as reported in the most of literature from the past.[12,23,24]

To evaluate the systemic association of OLP, many studies have been conducted in the past. Association of OLP and hepatitis C virus (HCV) in southern Europe and in Asia, has also been reported in literature.[24-27] The presence of HCV-specific T-cells in the oral mucosa of patients with chronic hepatitis C and OLP has also been found.[28] Although OLP patients do not appear to have an increased risk of diabetes, diabetics who develop OLP have an increased frequency of atrophic-erosive lesions and a greater proportion of lesions on the tongue.[29] In the recent past, many other associations have been reported especially dyslipidemia and glucose metabolism disturbance.[30,31] Siponen *et al.*[32] carried out a retrospective case-control study to test the association of OLP with thyroid disease in a Finnish population.

The data obtained in our study showed deranged TFTs in 9 out of 50 patients belonging to the OLP group, these included 5 female patients and 4 male patients, comprising 18% whereas only 1 patient from the control group i.e., 2% of the control group showed a deranged thyroid profile and on comparing the outcome of TFTs in two groups (OLP group and control group). Statistically significant difference was obtained with the $P < 0.05$.

CONCLUSION

The results obtained in our study demonstrate that a significant percentage of patients diagnosed with OLP have an association with thyroid gland dysfunction. However, it is impressed on that further studies are need to be carried out, involving a larger sample size, belonging to a different geographical strata so as to establish the association and the possible mechanisms.

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Original Article

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Management of Simple Ovarian Cyst with Ultrasonography Guided Aspiration and Sclerotherapy with Tetracycline

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Abstract

Introduction: The majority of ovarian cysts are symptomless and regress spontaneously. Until recent times, surgery has been the first treatment of choice. Cyst aspiration without the use of a sclerosing agent results in a higher recurrence rate, and hence the use of a sclerosing agent, such as tetracycline, methotrexate, or ethanol, is preferred.

Purpose: To evaluate the feasibility, efficacy and safety of tetracycline as a sclerosing agent in the management of simple ovarian cyst.

Materials and Methods: A total of 70 women having simple ovarian cyst were subjected to transabdominal cyst aspiration followed by 5% tetracycline sclerotherapy under ultrasonography guidance. Under local anesthesia, the cysts were punctured using spinal needle (18-gauge) and the contents aspirated. The aspirate was sent for cytological examination in all cases. Approximately, one-tenth of the aspirated cyst fluid volume was replaced with 5% tetracycline. Follow-up of the women was done clinically and using ultrasound initially twice weekly until the tetracycline is absorbed and then every 3 months for a period of 12-month to look for recurrence.

Results: Out of the 70 women all had serous aspirate. The result of cytological evaluation demonstrated benign lesion. On follow-up, 60 women showed complete resolution of cysts on ultrasonography. 10 women showed recurrence at various intervals which were then subsequently reaspirated. On follow-up, no recurrence was noted in them. χ^2 test shows that size of the cyst has a significant association (P = 0.01) with recurrence of cyst.

Conclusion: Management of simple ovarian cyst with ultrasonography guided aspiration and sclerotherapy with tetracycline is a safe, feasible and effective with minimal chances of recurrence and is a valid alternative to surgery.

Key words: Aspirations, Ovarian cysts, Sclerotherapy, Tetracycline, Ultrasonography

INTRODUCTION

An ovarian cyst is a thin walled collection of fluid which is larger than 2-3 cm.[1] The majority of them are symptomless and regress spontaneously. Some of them require treatment in the form of oral contraceptive pills. If untreated complications such as rupture, torsion, malignant transformation may occur.[2] Hence, surgical or interventional treatment is recommended. Until recent times, surgery in the form of laparotomy or laparoscopy has been the first choice.[3] However, ultrasonography guided aspiration of the cysts as an alternative treatment is the fast catching up and may even be procedure of choice in the management of ovarian cysts in a selected group of women as it has low recurrence rate, low risk, less cost and in most cases no hospital stay.[4] Surgery may even be considered Asan over treatment as most cysts

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are either benign or functional.[5,6] Cyst aspiration without the use of a sclerosing agent results in a higher recurrence rate and hence the use of a sclerosing agent, such as tetracycline, methotrexate, or ethanol, is preferred. Various studies have evaluated the feasibility of tetracycline as a sclerosing agent with good results.[7-9] The current study is to evaluate the therapeutic efficacy of aspiration and sclerotherapy with tetracycline of ovarian cyst.

MATERIALS AND METHODS

The prospective study was conducted in the Department of Radio diagnosis, Pt. J. N. M. Medical College, Raipur, India from August 2004 to July 2014. After obtaining a fully informed written consent, all women who fulfilled the inclusion criteria were included in the study.

The inclusion criteria for simple ovarian cystic were as follows:

- Unilocular
- Anechoic
- Wall thickness (<5 mm)
- Size >5.0 cm
- Without septations
- Without papillary projections or mural nodule
- Persistence of the cyst for at least 2 months.

The exclusion criteria were:

- Multilocular cysts
- Cysts with echoes and septations
- Ovarian cysts which were having papillary projection or mural nodule
- Cyst wall thickness > 5 mm
- Size <5 cm
- Tumor marker result (CA 125 > 35 ml/U per l)
- Pregnant women
- Women having known allergy to tetracycline.

After an overnight, fasting patients were taken for the procedure. The part preparation was done followed by painting and draping with betadine and spirit. Local anesthesia (2% xylocaine) was infiltrated at puncture site. An 18-gauge lumbar puncture needle was directed under sonographic guidance using 3.5 MHz transducers (Prosound 4000, Aloka, Japan); transabdominally to punctured ovarian cysts by freehand technique (Figures 1 and 2). The contents of the cyst were aspirated. The aspirated contents were sent for cytological examination. Then, 5% tetracycline was injected into cyst cavity, which was 10% of the aspirated volume (Figure 3). The women were managed on an out-patient basis, and all women received post-procedure analgesic and antibiotic coverage for a period of 3-day. The women were advised to attend regular follow-up visits (Figure 4). An ultrasound examination was performed twice weekly until tetracycline was absorbed, and then every 3 months for a year to check for recurrence. A cyst was considered to be recurrent if it was of diameter more than 5.0 cm.

RESULTS

The study included 70 women in the age group of 16-52 years with mean age 25.6 years. The mean size of cysts

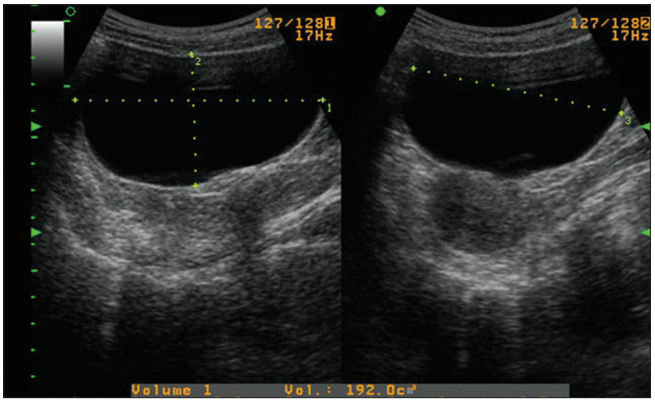

Figure 1: Transabdominal Ultrasound image of left ovary shows unilocular, anechoic simple ovarian cyst

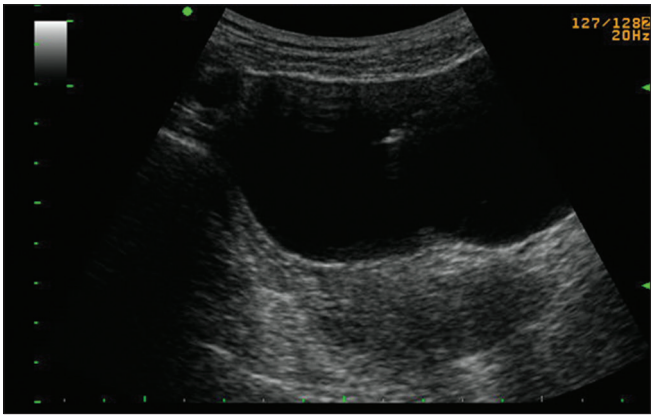

Figure 2: Tip of 18-gauge lumber puncture needle inside the left ovarian cyst

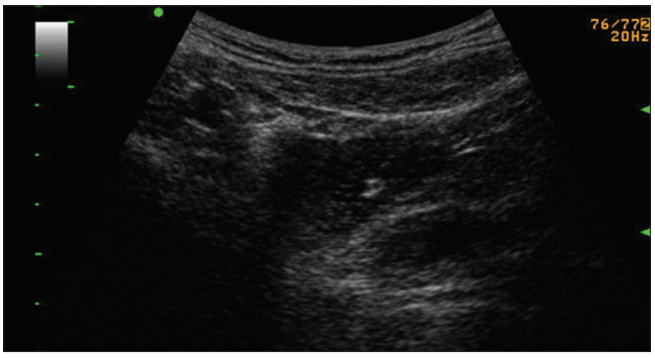

Figure 3: Ultrasound image shows post aspiration of cyst and injection of tetracycline producing internal echoes in the cyst

was 7.0 cm with range from 5.5 to 13.0 cm. The volume of the cysts ranged from 75 to 640 cc. The aspirate was serious in all women. The result of cytological evaluation demonstrated benign lesion in serious aspirates. The procedure of aspiration was performed once in 60 (85%) women and twice in 10 (15%) women. No immediate or post-procedural complications were noted. Follow-up after 3 months showed recurrence in six cysts of larger size (Tables 1 and 2). Rest of the women showed a significant reduction in size of cyst as compared to pre-procedural state. 6 months follow-up showed recurrence in none of the women; however at 12 months follow-up four cysts having larger size showed recurrence. Overall, resolution of cyst was observed in 85% of women with recurrence in 15% of women. χ^2 test shows that age is an insignificant factor ($P = 0.12$) and size of the cyst (>10.1 cm) has a significant association ($P = 0.01$) with recurrence of cyst considering $P < 0.05$ as significant.

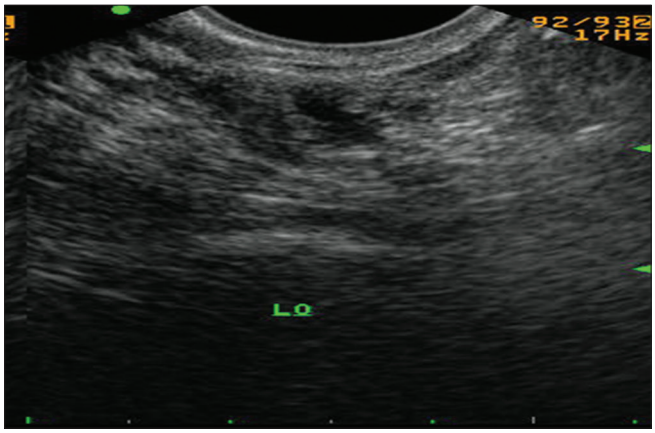

Figure 4: Transvaginal image shows resolution of left ovarian cyst at fifteen days follow-up

Table 1: Distribution of women according to outcome and age

Age group (years)	Number of women	Cyst resolution in percentage	Cyst recurrence in percentage
16-25	25	33	4.5
26-35	20	24	3
36-45	14	17	4.5
46-55	11	11	3
Total	70	85	15

Table 2: Distribution of women according to outcome and cyst size

Cyst size (cm)	Number of women	Cyst resolution in percentage	Cyst recurrence in percentage
5.5-7.0	8	11	0
7.1-8.5	22	28	3
8.6-10.0	20	26	3
10.1-11.5	12	13	4.5
11.6-13.0	8	7	4.5
Total	70	85	15

DISCUSSION

With the use of ultrasonography in recent years, there has been an increase in the detection of ovarian cysts majority of them being symptomless. However, treatment is required to avoid the potential complications. Surgery was the mainstay treatment until recent times, but ultrasound guided aspiration has proved to be a simple, effective, and rapidly effective treatment requiring no sedation in most cases.[10] Our study clearly indicates that management of ovarian cysts with aspiration and tetracycline injection is an effective method in its management. Complete resolution in 60 of 70 (85%) women on the first attempt and 10 of 10 women on the second attempt (100%). Many authors have used different sclerosing agents such as tetracycline, ethanol, and methotrexate. In this study, we used tetracycline due to its easy availability in our setting. No complication from tetracycline or from inadvertent spillage of tetracycline was noted. The cyst wall cells are responsible for the secretion of fluid and hence we employed tetracycline to cause fusion of the walls and prevent any recurrence.[11] There is a theoretical risk associated with aspiration of cysts which is seeding of the needle tract and the spread of malignant cells leading to dissemination.[12,13] To avoid this our inclusion criteria consisted of cysts which showed no features of malignancy on ultrasound. We also performed cytological examination of the aspirate to confirm the sonographic finding, and none of the cysts turned out to be malignant.

Fisch *et al.*,[14] reported complete resolution in 75% of women at follow-up examination and repeat aspiration of watery fluid was required in 25% of women and concluded that sclerotherapy with 5% tetracycline is a simple and effective alternative to surgical intervention. Kars *et al.*,[15] and Thummalakunta and Panditi[16] investigated the value of tetracycline sclerotherapy for management of recurrent or persisting non-neoplastic ovarian cysts in comparison to the aspiration without sclerotherapy and concluded that the use of a sclerosing agent leads to less recurrence. Abosrie and Abdelaziz[8] also showed that aspiration and sclerotherapy of ovarian cyst is a safe and effective treatment with a significantly low recurrence rate compared to simple aspiration only. In our study, the recurrence rate was 15% which we attributed to the cyst size. χ^2 test shows that age is an insignificant factor ($P = 0.12$) and size of the cyst (>10.1 cm) has a significant association ($P = 0.01$) with recurrence of cyst. Studies have shown parameters in predicting recurrence such as age, size of cyst and sidedness.[17]

CONCLUSION

In our study, we found that aspiration of simple ovarian cyst followed by tetracycline sclerotherapy is a safe, feasible and effective with minimal chances of recurrence and is a valid alternative to surgery.

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Original Article

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Role of Drainage Clamping For the Control of Blood Loss in Cemented Bipolar Hemiarthroplasty

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Abstract

Introduction: To reduce hematoma and blood loss in cemented bipolar hemiarthroplasty, drainage has been a regular practice. This study is aimed at evaluating the outcome of clamped drainage in blood loss and wound healing following cemented bipolar hemiarthroplasty.

Materials and Methods: A total of 40 patients with fractured neck of femur operated with cemented bipolar hemiarthroplasty, who underwent a prospective cohort study, were randomized equally into two groups: 6 h post-operative clamped and non-clamped suction drainage. Gender distribution, pre-operative hemoglobin levels, hip pathology, and affected side were comparable and were recorded between the two groups.

Result: Blood loss and calculated blood loss volumes were recorded higher for the non-clamped patients. Almost 110 ml blood loss was noticed more in the non-clamped patient group. No significant difference in adverse events or need for transfusion noticed.

Conclusion: This study showed a statically significant reduction in post-operative drainage amount between clamped and non-clamped drainage groups; however, this difference was not large enough to warrant increases blood transfusion requirements in patient with unclamping drainage.

Key words: Blood, Drain, Fracture, Hemiarthroplasty

INTRODUCTION

In fractured neck of femur, cemented bipolar hemiarthroplasty has been widely applied. Cemented bipolar hemiarthroplasty has relieved pain, corrected deformity and has restored and improved joint movement, thus making it widely accepted surgery by patients and performed by an orthopedic surgeon. A volume of 1000-2000 ml of blood loss has been associated in this surgery in lieu of extensive soft tissue and bone dissection.[1-3] Hematomas are due to the lack of complete hemostasis as there is exposure of medullary canal, increase wound tension, decrease in soft tissue perfusion all of these leads to hampering of wound healing. There is an increased risk of deep vein thrombosis (DVT), longer hospital stay, surgical procedures (subsequent), and increase health care economic burden due to prolonged wound drainage.[4] Skin temperature was lower in drainage site was found by Koyano *et al.* by performing wound skin temperature thermography, and thus suggested that drainage can suppress inflammation.[6] Lower infection rates were observed by Waugh and Stinchfield when drainage was used, thus decreasing list of hematoma formation and wound tension.[5] These all have promoted wound healing and functional joint recovery.[7] Contraindicately, this results have not been found similar promising in other studies with or without closed suction drainage.[5,8-10] Since the results on the use of drainage remains doubtful; definite information is mandatory to achieve patients expectations and desired outcomes.[11,12] In total, knee arthroplastic surgeries data have been reported that clamping drainage can reduce blood loss and the need for blood transfusion post-surgery in cemented bipolar

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hemiarthroplasty and no such similar reports have been reported. Henceforth, we have conducted this study to emphasize the role of clamping the drainage for 6 h post-operatively to a better management of post-operative cemented bipolar hemiarthroplasty by reducing blood loss and minimizing post-operative complications.

MATERIALS AND METHODS

Patients with fractured neck of femur who underwent cemented bipolar hemiarthroplasty between May 2014 and August 2015 were included in this study. Patients with previous history of hip surgery, current infection, and medical ailments contraindicating surgery were excluded from this study. Using a random number list generated by the computer, patients were randomly allocated who meet the inclusion criteria. The surgeons who performed the surgery were unaware of the patients grouping into clamped and non-clamped drainage. Patients were unaware of their drainage tube clamping or non-clamping. All the anticoagulation's were stopped 1 day prior to the surgery. All patients, who underwent the surgery, were positioned in lateral decubitus position and were operated via posterior approach under spinal anesthesia by the same surgical team. 30 min to prior to surgical skin incision, 1 g of cefrtriaxone was given. Short external rotators muscles were sutured back after the surgical procedure, the wound closed with a drainage tube placed under the deep fascia. After this, patients were randomized either under clamped drainage group or the non-clamped drainage group based on formal randomization. The drainage in the clamped group was kept clamped for the first 6 h post-operatively. Non-steroidal anti-inflammatory drugs were used as analgesia post-operative. Surgical wounds and drain were checked at the 2nd day, and then, it was removed in both groups. Quads strengthening and extension-flexion movement were encouraged immediately after surgery under the guidance of a trained physiotherapist. Blood loss parameters were the main results of interest in this study.Immediately and 48 h post-operatively, hemoglobin (Hb) levels were measured. According to Gross, total blood loss was calculated based on maximum perioperative decrease in Hb. The drainage blood was recorded when the tube was removed 24 h post-operatively. Hb levels <9 g/dl are an indication for the blood transfusion. Within the initial 6 weeks post-operative period, adverse events such as delay in wound healing and recovery due to hematoma redness of the incision, superficial or deep infection, and DVTs recorded. Any deep infection was diagnosed based on a positive culture from the wound. Continuous data were expressed as mean ± standard deviation and tested with Student's *t*-test for difference. The Chi-square test was used to analyze the categorical data. $P < 0.05$ was considered to be statically significant.

RESULTS

A total of 40 patients were recruited into the study. There were 12 women and 9 men in the clamped group with the mean age of 63 ± 4.5 years with a body mass index of 25.8 ± 2.1 kg/m^2. Affected side was left in 10 cases unclamped and for 10 in the clamped group and right for 8 cases unclamped and for 12 in the non-clamped group. Pre-operative Hb was 13.5 ± 1.0 and 13.1 ± 2.1 g/dl for the clamped and non-clamped, respectively. No statistical significant difference between these two groups for these parameters. The drainage blood was recorded, and the Hb level was tested 24 h after the tube removal. The drainage blood measure was 157.3 ± 16.3 and 243.3 ± 60 ml in the clamped and non-clamped group with Hb 10.9 ± 1.2 and 10.3 ± 1.0 g/dL ($P = 0.021$) for each group. The calculated blood volumes were 1040 +/- 110.2 ml for the clamped group and 1320 ± 140 ml for the non-clamped group ($P = 0.012$) (Table 1).

Transfusion was performed for the one patient in the clamped group and four patients in the non-clamped group that was not a significant difference ($P = 0.287$). Two superficial, three hematomas, and two redness of incision in the clamped group, while one superficial, two hematomas, and one redness of incision in the non-clamped grouped found. No statically significant between the two groups was found for adverse events ($P = 0.461$).

DISCUSSION

Just like in the total knee arthroplasty (TKA), the effect of closed suction drainage on blood loss and wound complication has been arguable in the cemented bipolar hemiarthroplasty. Certain randomized studies and meta-analysis have not been in favor of the routine use of drainage.[10-15] Kim *et al.* did find a correlation between the incidence of wound complication and the use or nonuse of closed-suction drainage.[7] Various types of drains have been analyzed in the TKA with promising effects on reduction of blood loss and the need for the blood transfusions.[13,16] Releasing the tourniquet has significant influence on the blood flow in a short time after the reestablishment of the

Table 1: Comparison of various parameters in the respective group

Parameters	Clamped	Unclamped
Drain (ml)	157.3±16.3	243.3±60
Hb (g/dL)	10.9±1.2	10.3±1.0
Blood volume (ml)	1040±110.2	1320±140
Blood transfusion	1	4
Hematomas	3	2
Adverse events	None	None

Hb: Hemoglobin

blood flow.[17] It has been found that clamping for a short time can provide the same effect as persistent drainage under the compression of elastic bandage after the tourniquet release.[16] Cemented bipolar is different from TKA as it is impossible to compress the wound and use a tourniquet. Regional pressure acts to stop blood loss and clamping the drainage, the drainage post-operatively may result in great pressure, thus contributing to hemostasis.[18] Just like in total knee replacement, the ideal duration of clamping is uncertain from the literature; however, a longer clamping duration has been associated with delayed wound healing, skin edge necrosis, hematoma, and increased risk of infection.[16,19] compared to the non-clamped group, the in wound problems or post-operative complications in the clamped group is the same. The most ideal result in the less blood loss and the need of blood transfusion without complication of wound healing resulting from hematoma. In this study, 6 h clamping period can reduce post-operative blood loss by 100 ml without more wound problems. Longer clamping time for 8 h or 12 h may be tested in further studies. Short post-operative period is the shortcoming of this study.

CONCLUSION

The purpose of this study was to conclude if post-operative clamping had an effect on blood loss, post-operative complications, and Hb levels after cemented bipolar hemiarthroplasty. The result of our study suggested that clamped drainage for 6 h post-operatively could reduce post-operative blood loss without an increase in wound healing complications or other post-operative complications as compared with the non-clamped drainage. Further study has been under investigation to further increase the period of clamping time and their efficient consequences.

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Original Article

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Prevalence of Hypothyroidism in Females with Exodontia: A Randomized Prospective Study

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Abstract

Introduction: Primary hypothyroidism is a condition characterized by the failure of the thyroid gland to produce sufficient thyroid hormones. Thyroid hormones play an important role in the regulation of growth, development, and metabolic functions of the body.

Objectives: Hypothyroidism and diabetes mellitus are the two most common endocrine disorders in clinical practice. The aim of this study was to estimate the prevalence of hypothyroidism and diabetes in patients visiting to oral and maxillofacial surgery department for tooth extraction.

Materials and Methods: This study was conducted in the department of oral and maxillofacial surgery for 1 year. Patients for this study were selected from among the ones who attended the OMFS department for teeth extraction and were on medication for hypothyroidism and diabetes. Patients were divided into two groups. Group A patients having hypothyroidism Group B having hypothyroidism and diabetes.

Results: Hypothyroidism was seen in 284 males (20.10%) whereas 568 (79.89%) females. Diabetes was seen in 33.92% males and 66.07% were females. Both hypothyroidism and diabetes was seen in 32.5% males and 67.5% females complications in both groups following things were noted. In 60% intraoperative bleeding was encountered, wound infection and dry socket was found in 35% delayed wound healing was noted in 32% patients, post extraction swelling and pain in 65% of cases.

Conclusion: The percentage of hypothyroidism and diabetes in females is much higher than males. We suggest that routine screening of population, especially females between 30 and 60 years of age should be done, and healthy stress-free lifestyle be practiced.

Key words: Diabetes, Dry socket, Extraction, Hypothyroidism, Thyroid stimulating hormone

INTRODUCTION

The shape of thyroid gland resembles butterfly at the base of the neck and it produces several hormones. Thyroid gland produces two very important thyroid hormones, thyroxin called thymoglobulin thyroxin T4. It is an inactive hormone, and is a reserve supply.[1] In our circulation 95% hormone is T4, 5% is triiodothyronine T3. As per experts, T3 is the true and more powerful hormone than T3. Both hormones are attached to the protein called thyroxin - binding globulin and are measured as total T3 and T4.[2]

The pituitary gland produces thyroid stimulating hormone or (TSH). This hormone stimulates the thyroid gland to increase the production of thyroid hormones. A high TSH determined by blood tests indicates that thyroid is under active and needs stimulation. While a low TSH means the thyroid is overactive. The thyroid gland is constantly reacting to the changes in the level of circulating TSH.[3] The alterations in the level of circulating TSH[3] causes constant reactions in the thyroid gland and thyroid problems arise as a result lack of response to TSH, faulty TSH secretions and thyroid releasing hormones, failure to produce thyroxin from thyroid gland or thyroid becomes autonomous (part or whole gland produce thyroxin without reacting to

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TSH changes).[4] The thyroid regulates the metabolism of the body cells, emotions, appetite, mood, cognition, and behavior.[5] Females are more affected with thyroid diseases than males in incidence. Thyroid has two lobes right and left that is situated anterolaterally on the trachea.[6]

Hypothyroidism results when thyroid gland releases an excess amount of its hormones in short (acute) or long (chronic) period of time. 15% of the population show abnormalities of thyroid gland anatomy on physical examination as per estimated records.[7]

When thyroid gland fail to synthesize enough thyroid hormone or when it fails to function adequately resulting in reduced amount of thyroid hormone in the body, is known is hypothyroidism.[2] Hypothyroidism results from either the disease outside the gland such as low intake of iodine, or deficiency within the gland like inflammation causing destruction of gland cells. Hashimoto's thyroiditis is a condition resulting from destruction of the gland, is autoimmune and results from the attack of the immune system on gland cells. Some females develop this condition after pregnancy and are called as postpartum thyroiditis.[8]

Other causes of hypothyroidism are radioactive iodine, surgical removal of the gland, diabetes,[9] infertility,[10] obesity,[11] and certain drugs like lithium. In iodine rich countries like United states and Japan most common cause is Hashimoto's thyroiditis.[12]

Patients with hypothyroidism are more susceptible to cardiovascular diseases (CVS). Suitable coagulation test is advised to the patients if they are on thyroid replacement and anticoagulants, physician should be consulted for such patients.[9,10]

Dental surgical procedures should be avoided in patients who show severe stress or infection, abnormal weight gain, mental sluggishness, frog-like husky voice, and edematous appearance of the whole body called myxedema.[1,3,5]

The most common oral findings of hypothyroidism are macroglossia, dysgeuses, poor periodontal health, delayed wound healing and delayed eruption, impactions, this may be due to lack of space for a proper eruption.[13]

Thyroid disease is very common in general population ranging from 6.6% to 13.4% whereas in diabetic patients the prevalence is still greater and varies from 10% to 24%.

MATERIALS AND METHODS

The prospective study was conducted in oral and maxillofacial surgery department. The patients who reported for extraction of teeth with a history of hypothyroidism were included in the study (self-reported). Clinical symptoms such as husky voice, excess weight gain, CVS diseases and hypertension, diabetes, history of any drug intake such as anticoagulants, antidepressants, delayed wound healing, and bleeding disorders, were noted. Patients were divided into two groups. Group A included hypothyroid patients alone. Group B included patients with hypothyroidism with diabetes, hypothyroid and hypertension. Investigations such as bleeding time, clotting time, other coagulation tests, blood sugar, T3, T4, and TSH, were advised before extraction.

RESULTS

Total cases of extractions from January 2014 to December 2014 were 15961. Total males - for extraction 8786 (56.20%), total females for extraction 7175 (43.79%) females.

The TSH value above 4.3 to10 mU/l was taken criteria. Hypothyroidism was seen in 284 males (20.10%) whereas 568 (79.89%) females (Figure 1).

Hypothyroidism alone seen in 33.92% males and 66.07% were females. Both hypothyroidism and diabetes was seen in 32.5% males and 67.5% females (Figure 2).

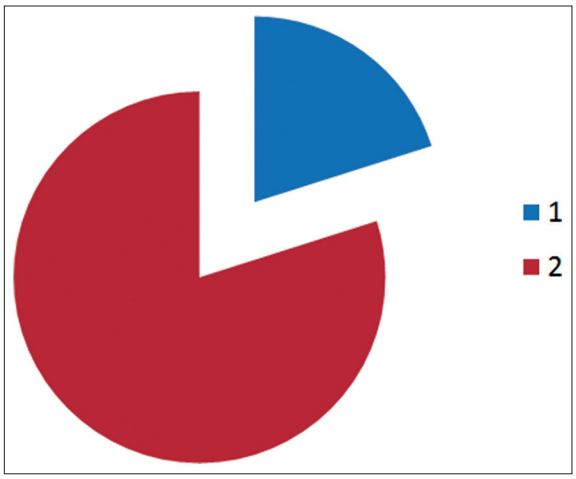

Figure 1: Pie chart 1 males 2 females

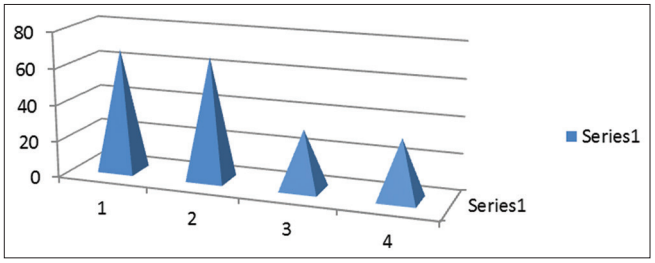

Figure 2: Male, female thyroid, diabetic and both ratio

Complications in both groups following things were noted wound infection/dry socket was found:

- Intra operative bleeding 60%
- Wound infection/dry socket was found 35%
- Delayed wound healing was noted in 32
- Pain and swelling in 65%
- Post-operative bleeding in 2% (Figure 3).

DISCUSSION

India has been given the status of "optimal iodine nutrition" in 2004 by WHO assessment of global iodine.[14,15] 83.2% urban and 66.1% of the households now consume adequately iodized salt.[16,17]

Recent studies have conducted in post iodization phase which has shown a transition from iodine deficiency state and an indication of a corresponding change in thyroid status of the Indian population.[18] However, most of the studies are limited to certain geographical areas or cities similar to this study sample among them 852 patients were suffering from hypothyroidism (self-reported).

Thyroid disorder is the most common disorder of the endocrine system and is increasing predominantly in women.[19] Females suffer more than males up to 5% of the females have altered thyroid function.[20,21] This study also shows females suffering more them males (568 females and 284 males). Our study is consistent with worldwide reports particularly in midlife (45-55). As per studies, thyroid disorders are associated with cardiovascular risk factors such as hypertension and dyslipidemia.[22]

The two most common endocrine diseases are hypothyroidism and diabetes mellitus.[23] In 1979, the association of these two diseases was published.[24] Several studies have been conducted in different countries to show an association between two diseases. There is great variability in the prevalence of thyroid diseases in diabetic patients from 6.6% to 13.4%.[25,26] In our study hypothyroidism alone was seen in 33.92% males and 66.07% were females whereas diabetes and hypothyroidism were found 32.5% males and 67.5% females. Both the diseases were predominantly in women 67.5% (Figure 2). The prevalence figures noted women in this study draw attention to the growing health needs of this segment of Indian population.

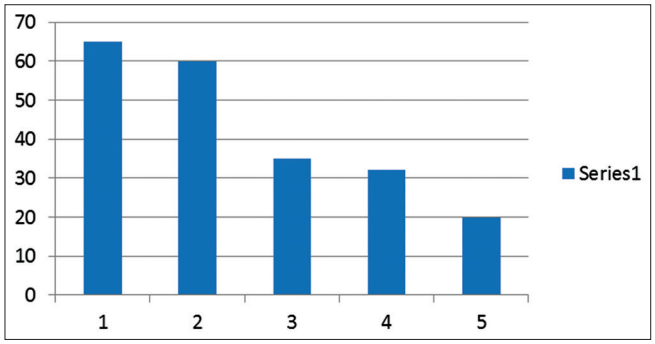

Figure 3: Post extraction complication associated with patients of hypothyroidism

Post extraction bleeding was noticed more in hypothyroid patients (60%) in comparison to normal patients. This may be because of excess subcutaneous mucopolysaccharides subcutaneous which decreases the ability of small blood vessels to constrict, resulting in excessive bleeding from in filtered tissues including mucosa and skin.[27] Bleeding was controlled by digital pressure packs. Post extraction pain, the swelling was seen in 65% of the cases whereas in 2% cases post-operative bleeding was seen (Figure 3).

Susceptibility to infection delayed wound healing is a very common feature of hypothyroidism, which may be due to decrease in metabolic activity in fibroblasts and increased risk of infection because of longer exposure of the wound to the pathogenic organisms. In this study, delayed wound healing in 32% and dry socket was present in 35% of cases in the present study (Figure 3).

Hypothyroid patients are more susceptible to cardiovascular diseases from arteriosclerosis and elevated LDL. Patients who are on anticoagulant therapy were given antibiotic prophylaxis depending on the severity for any invasive procedures.[28]

Drug interactions of L-thyroxin include increased metabolism due to phenytoin, rifampicin, carbamazepine tricyclic antidepressants, iron sulfate, iodine. It also increases the effect of warfarin sodium.[29] Appropriate coagulation tests should be done in patients on anticoagulants and hormone replacement therapy.

CONCLUSION

Thyroid hormone have an important role on metabolism, regulating myocardial functions, homoeostasis, pulmonary ventilation, mentioning vascular tone thus having a wide variety of actions in almost all systems of human body. Hypothyroidism and diabetes are two common endocrinal disorders in Indian population, especially in females in middle and older age groups. In a significant number of patients autoimmune mechanism appears to be a main etiologic factor. Our study had limitations because it was conducted in a small group of the population.

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Original Article

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"Filarial Dance Sign" with Cytological Detection of Microfilaria: Our Experience over a Two-Year Period

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Abstract

Introduction: Filariasis is a major health problem in tropical countries including India. Adult worms of *Wuchereria bancrofti* reside in the lymphatics and cause progressive lymphatic vascular dilation and various pathologic lesions in organs such as lower limbs, spermatic cord, epididymis, testis, retroperitoneum, and rarely in the female breast. Adult worms can be demonstrated on real-time ultrasound (USG) by their characteristic wriggling movements known as "filarial dance sign" (FDS). Demonstration of microfilariae in fine needle aspiration cytology (FNAC) smears of the swellings with FDS play an important role in the prompt diagnosis of the disease.

Purpose: The current study aims to assess the role of FNAC in demonstration of microfilaria in the cases which showed "FDS" on real-time high-resolution ultrasonography.

Materials and Methods: A total number of 13 cases comprising breast swelling, scrotal swelling, and inguinal swelling showing FDS on real-time high-resolution ultrasonography were subjected to USG guided FNAC for demonstration of microfilaria.

Results: Of 13 cases, five cases were of breast swelling, six cases were of scrotal swelling, and two cases were of inguinal swelling. Filarial dance was demonstrated in ultrasonography in all the cases. On FNAC, adult gravid female worm with eggs and microfilaria were seen in one case of breast swelling and one case of scrotal swelling; microfilariae were detected in two cases of breast swelling, five cases of scrotal swelling and both the cases of inguinal swelling.

Conclusion: High-resolution ultrasonography is a useful technique for diagnosing not only inguino-scrotal filariasis but also filariasis of the breast. USG guided FNAC in these patients can lead to prompt diagnosis of the disease and initiation of treatment.

Key words: Breast, Filariasis, Fine needle aspiration cytology, Microfilaria, Ultrasonography, *Wuchereria bancrofti*

INTRODUCTION

Lymphatic filariasis affects more than 120 million people worldwide, and WHO has identified filariasis as the second leading cause of permanent and long-term disability after leprosy.[1,2]

Lymphatic filariasis in humans is commonly caused by human parasitic nematode *Wuchereria bancrofti* along with *Brugia malayi* and *Brugia timori*.[1] Filariasis of skin and subcutaneous tissue is caused by Onchocerca volvulus and *Loa loa*.

In endemic areas, filariasis causes a spectrum of diseases including (1) asymptomatic microfilaremia, (2) recurrent lymphadenitis, (3) chronic lymphadenitis with swelling of dependent limb or scrotum (elephantiasis), and (4) tropical pulmonary eosinophilia.[3]

Adult worms of *W. bancrofti* reside in the lymphatics and cause progressive lymphatic vascular dilation and various pathologic lesions in organs such as lower limbs, spermatic cord, epididymis, testis, retroperitoneum, and rarely in the female breast.[4,5] A majority of infected individuals in filarial endemic communities are asymptomatic.

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Filariasis of the breast is a rare cause of breast lump.[2] It is a cause of concern as the patients with breast filariasis presenting with lump are often clinically suspected to be malignant. Genital filariasis in India presents commonly as secondary vaginal hydroceles. Adult filarial worms can be demonstrated in the dilated lymphatics on real-time high-resolution ultrasound (HRUS), by their characteristic wriggling movements known as "filarial dance sign" (FDS).[6,7] FDS is a diagnostic sign of inguino-scrotal filarial infection and breast filariasis.[6,8]

Conventional mode of diagnosis of filariasis is by demonstration of microfilaria in peripheral blood smear. Despite high incidence, it is infrequent to find microfilariae in fine needle aspiration cytology (FNAC) smears and body fluids. There have been reports of incidental detection of microfilariae in FNAC smears and body fluids.[5,9] The current study aims to assess the role of ultrasound (USG) guided FNAC in demonstration of microfilaria in the cases which showed "FDS" on real-time ultrasonography.

MATERIALS AND METHODS

The study was conducted at the Department of Pathology in collaboration with the Department of Radiology at Rama Medical College, Hospital and Research Centre, Mandhana, over a period of 2-years from September 2013 to August 2015.

The study group comprised 13 patients in whom the FDS was seen on real-time HRUS with use of 10 MHz linear probe. Of thirteen cases, five cases were of breast swelling, six cases of scrotal swelling, and two cases were of inguinal swelling. Both the cases of inguinal swellings were male patients.

With the patient in the supine position, all swellings were scanned with high-resolution ultrasonography. Doppler imaging was used to for delineation of lymphatic vessels/spaces for differentiation from blood vessels. Both real-time video and still images were stored on hard drive with recording of microfilarial movements. All 13 patients were subjected to USG guided fine-needle aspiration, after taking consent. FNAC was done by 22-23 G needle attached to 10 ml syringe. The needles were placed in the areas which had positive findings for the FDS. Alcohol-fixed smears were stained with Hematoxylin and Eosin stain and air-dried smears were stained with Leishman stain. Routine blood counts and peripheral smears for microfilaria were obtained from all patients.

RESULTS

Of 13 cases with "FDS," five cases (38.5%) were of breast swelling, six cases (46.1%) were of scrotal swelling, and two cases (15.4%) were of inguinal swelling. Clinical details and age distribution of patients were variables (Table 1). Of five cases of breast swelling, in three cases left breast and in two cases right breast was involved. The patients with breast swelling (four out of five) were predominantly in the fourth decade and were diagnosed clinically as fibrocystic disease. One patient with breast swelling was 55 years old, and clinically a suspicion of malignancy was raised. Of six cases of scrotal swelling, two involved the left side, and four involved the right side. Two patients also had a hydrocele. Both the inguinal swellings were on the left side. Peripheral blood smear and cytologic findings are discussed in Table 2.

High-resolution ultrasonography of breast swellings showed well-defined cystic lesions in all the cases. In two cases, multiple cystic lesions were seen. All the cysts were well-defined and thin walled. The largest cyst measured 2.5 cm × 1 cm, and the smallest cyst measured 1 cm × 0.8 cm. In all five cases, the cyst cavity showed linear echogenic structure. The elongated worm showed slow, repetitive dancing movements on real-time ultrasonography. No calcification was obvious in the cyst. A diagnosis of breast filariasis with live adult worm was suggested. On USG guided FNAC, adult gravid female worm with eggs and coiled microfilariae were seen in one case (Figure 1) of breast swelling. In two cases, cytology smears revealed microfilaria along with few inflammatory cells (Figure 2). Two cases (15.4%) did not show either microfilaria or adult worm in cytology smears.

Table 1: Clinical data of all the cases included in present study

Clinical data	Breast swelling	Scrotal swelling	Inguinal swelling
Number of cases	5	6	2
Clinical findings			
Age range (mean) year	32-55 (mean 40)	25-37 (mean 31.2)	15-26 (mean 20.5)
Swelling	5	6	2
Pain	5	4	-
Fever	2	4	1
Erythema	1	2	-

Table 2: PBS and cytologic findings of all the cases included in present study

PBS and cytology details	Breast swelling	Scrotal swelling	Inguinal swelling
Peripheral smear findings			
Eosinophilia	2	3	1
Microfilaremia	-	1	-
Cytologic findings			
Hemorrhagic aspirate	2	1	1
Fluid aspirate	1	2	1
Adult worm in aspirate	1	1	-
Microfilariae in aspirate	2	5	2
Polymorphs	2	2	1
Eosinophils	1	3	-

PBS: Peripheral blood smear

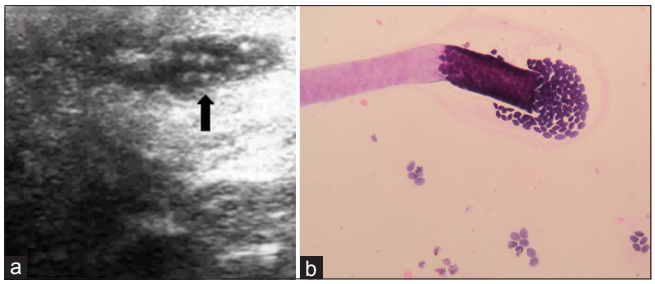

Figure 1: (a) B-mode high-resolution ultrasound of left breast showing well defined lobulated cystic lesion in upper outer quadrant showing internal actively mobile linear echogenic structures (filarial dance sign), (b) cytology smear from breast aspirate showing adult filarial worm with eggs (H and E ×100)

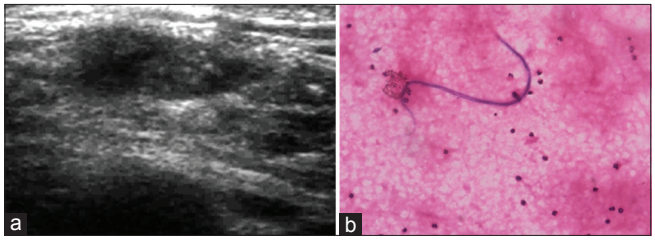

Figure 2: (a) High-resolution ultrasound of right breast showing well defined lobulated cystic lesion in upper medial quadrant with filarial dance sign, (b) cytology smears from breast shows microfilaria in a background of inflammatory cells (H and E ×400)

B-mode HRUS of scrotal swellings showed small, well-defined cystic lesions in the subcapsular region of testicular parenchyma and adjacent to epididymis with no flow on color Doppler study. Multiple, echogenic linear structures with a persistent rigorous wriggling motion were observed within these. Free fluid was observed in the scrotal sac in two cases. USG guided FNAC revealed adult worm with coiled microfilaria in one case (Figure 3). Rest five cases showed microfilariae in cytology smears. Peripheral blood smear revealed microfilaremia in one case of scrotal swelling.

HRUS of inguinal swellings showed dilated anechoic channels (lymphatics) with no flow on color Doppler study. Multiple actively motile elongated tubular structures were seen within these channels. USG guided FNAC revealed microfilariae in both the cases (Figure 4). In all the cases, the microfilariae showed the presence of hyaline sheath and well-separated nuclei with absence at the cephalic end and tail tip.

All the patients were followed-up after 3 weeks of oral therapy with DEC. Four patients (2 scrotal, 1 breast, and 1 inguinal swelling) were lost to follow-up. Rest all cases showed decrease in pain and swelling. On repeat ultrasonography, 3 patients of breast swelling, 2 patients of scrotal swelling, and 1 patient of inguinal swelling demonstrated no linear echogenic structures or movements.

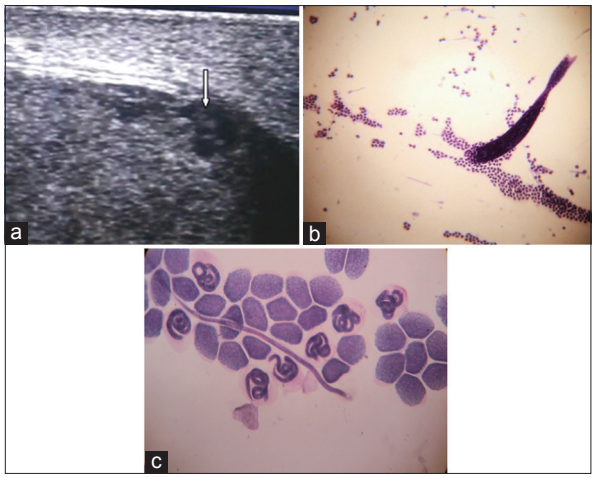

Figure 3: (a) B-mode high resolution ultrasound of left testes showing well-defined cystic lesion in subcapsular region with internal undulating tubular echogenic structures (filarial dance sign), (b) cytology smear from testicular aspirate shows adult female worm with eggs (H and E ×100), (c) cytology smear showing numerous microfilarial eggs, coiled microfilaria and an uncoiled microfilaria (H and E ×1000)

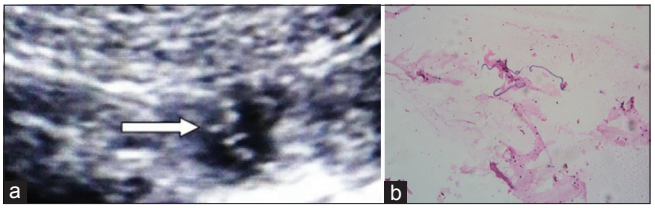

Figure 4: (a) Ultrasound of inguinal region showing well defined lobulated cystic lesion in left inguinal region with filarial dance sign, (b) cytology smear from inguinal swelling shows multiple microfilariae in a background of inflammatory cells

One patient of breast and scrotal swelling showed linear echogenic structures, but they did not have the movements.

DISCUSSION

Filarial infection is endemic in the tropics including India, part of Sri Lanka, Africa, and the Far East. There are eight species of filarial parasite, out of which only three, *W. bancrofti*, *Brugia malayi*, and *B. timori* are known to cause lymphatic filariasis.[10] 90% of all filariasis cases in the world are caused by *W. bancrofti*, followed by *B. malayi* and *B. timori*.[11]

Man is the definitive host, and the mosquito is the intermediate host for bancroftian and brugian filariasis. *Culex quinquefasciatus* transmit *W. bancrofti* and *Mansonia* mosquitoes transmit Brugian filariasis. The microfilaria of *W. bancrofti* and *B. malayi* display nocturnal periodicity.

Mosquitoes deposit infective larvae on the skin and transmit the infection. The larvae develop into adult worms over a

period of 6 months-2 years in the lymphatics. Adult worm produces microfilaria, which circulate in the blood stream.[12]

The majority of infected individuals in endemic areas remain asymptomatic throughout their life. Symptomatic patients may show an acute phase of disease characterized by fever, muscle pain, lymphangitis, lymphadenitis, and lymphedema. The chronic stage may be characterized by lymphadenopathy, lymphedema, hydrocele, and elephantiasis.

The lower extremities and genitalia are the most common sites of involvement, followed by the upper extremities. However, the organisms may be found in any organ of the body causing a mass lesion in the absence of the classic signs of filariasis.[13]

Breast filariasis is a rare cause of breast lump. It is the host inflammatory immune reaction, which is responsible for the wide spectrum of symptoms and signs associated with the filarial affliction of breast.[14] Intact worms produce minimal tissue reaction while degenerating parasites provoke inflammatory cell infiltration- mainly eosinophils and occasional development of epithelioid granulomas.[14]

Before the description of the FDS on ultrasonography, there were no methods available to detect adult filarial worms *in vivo*. By localizing the adult worms on ultrasonography, the response to therapy can be assessed. Amaral *et al.* first reported FDS in 1994.[15] They described the movements of live adult filarial worms in the lymphatic vessels as "peculiar, random-appearing movements of objects inside a vessel-like structure with persistent, random, twirling movements. This sign is unique and specific for filarial adult worms.

Chaubal *et al.* reported a series of eight cases of scrotal FDS.[9] In two patients, they aspirated the dilated lymphatic channels and demonstrated microfilariae in the aspirates. In the present study, 13 patients with scrotal, breast, and inguinal swellings demonstrated positive FDS. All the patients were subjected to USG guided FNAC, and in 11 patients, filariasis was confirmed by cytology smears. Earlier, there were single case reports for filarial dance in breast mass;[8] however, the present study shows five cases of breast swelling with FDS.

Despite the high incidence of this parasite in the endemic zone, detection of adult gravid filarial worm or eggs in FNAC is extremely rare. Kapila and Verma[5] and Azad *et al.*[16] reported the presence of adult filarial worms in soft tissue swellings. Chakrabarthi *et al.*[11] reported adult worm in breast lump aspirate. In our study on USG guided FNAC, adult worm were demonstrated in cytology smears in one case of breast swelling, and one case of scrotal swelling. Demonstration of microfilaria in FNAC smears is also an uncommon finding. In the present study, microfilariae were seen in cytology aspirates of nine cases. This finding confirms that USG guided FNAC in patients with positive FDS is an excellent tool for demonstration of microfilaria or adult worm. FDS on HRUS correlates with active release of microfilariae by the worms and hence indicates active infection. In two cases of breast swelling with FDS, microfilaria could not be demonstrated in cytology smears.

The response of adult filarial worms to diethylcarbamazine is demonstrated by many authors.[17] The response is quite variable in different patients, and even in the same patient, different adult worms may show varying response. Ultrasonography, being the only modality that can show the adult worms, is very useful in the follow-up period to document the response of worms to the drug. Complete absence of worm movements on follow-up examination was taken as a positive response. In our study, 8 (61.5%) of 13 patients had a positive response to the drug, which correlates with results from previous studies.

CONCLUSION

High-resolution ultrasonography is a valuable technique for diagnosing filarial infection in symptomatic patients. This study emphasizes on the importance of the classic and diagnostic USG finding of FDS. USG guided FNAC in the patients presenting with FDS helps in detecting microfilaria or adult worm and thus plays a significant role in recognition of the disease and institution of specific treatment. The appearance of motile filarial worms on ultrasonography correlates with active release of microfilariae into the lymphatic vessels and hence indicates active infection.

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Original Article

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Functional Outcome of Accelerated Rehabilitation in Arthroscopic Anterior Cruciate Ligament Reconstruction with Semitendinosis and Gracilis Graft

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Abstract

Introduction: An ideal rehabilitation program post anterior cruciate ligament (ACL) reconstruction enables an individual to return to pre-injury levels at a faster rate with minimal to no risk of reinjury to the graft.

Aim of Study: (1) The aim of our study is to assess the outcome of accelerated rehabilitation post-ACL reconstruction, (2) a rehabilitation program for a duration of 6 months is sufficient when compared to 9 months, (3) role of KT 1000 arthrometer in the diagnosis of ACL tears.

Materials and Methods: A total of 106 patients were operated by a single surgeon underwent arthroscopic anterior cruciate ligament reconstruction using quadrupled semitendinosis and gracilis graft and partial meniscectomy for associated meniscal tear. Patients were put on an accelerated rehabilitation protocol designed in our institute on the first post-operative day; under the guidance of a physical therapist in consultation with the operated surgeon. Patients were followed up at 3 weeks, 6 months, and 9 months post onset of rehabilitation; patients were assessed using KT 1000 arthrometer and Lysholm knee scoring system.

Results: Out of 106 patients, who were selected, 96 (91%) were males and 10 (9%) were females. The mean pre-operative Lysholm score was 55.09. Postoperatively while on accelerated rehabilitation program the Lysholm scores were 69.73 at 3 weeks, 89.13 at 6 months, and 89.19 at 9 months. In our pre-operative evaluation mean KT 1000 arthrometer score was 10.53 and post-operative at 6 months was 3.49. At 9 months, 105 patients had excellent results, whereas 1 patient had a good result.

Conclusion: Accelerated rehabilitation protocol enables the patient to functionally recover faster to pre-injury levels. A rehabilitation protocol for 6 months is sufficient in enabling a patient to get back to pre-injury levels. Functional outcome is the same with or without associated meniscal injuries. KT 1000 knee arthrometer plays a vital role in diagnosing ACL injuries and can be used to compare pre-operative and post-operative ligament status.

Key words: Accelerated rehabilitation protocol, Anterior cruciate ligament reconstruction, KT 1000 knee arthrometer, Lysholm knee score, Prospective study

INTRODUCTION

Anterior cruciate ligament (ACL) reconstruction restores knee function to pre-injury levels, without any pain. It also prevents degenerative changes in the knee. ACL, it also allows the patient to return to sporting activities.[1]

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The rationale for rehabilitation after an ACL injury is to gain a good functional stability, reach the best possible functional level and to decrease the risk for reinjury. The training programs are focused both on the injured leg, but also on the non-injured leg, hip, and trunk muscles that are needed to stabilize the entire body. The functional stability of the knee joint is dependent on the interplay of passive structures and the dynamic system. The ligament provides

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an average of 86% of the total resisting force to anteriorly directed forces on the tibia.[1]

Rehabilitation protocols have changed considerably over time in the past. It has become "aggressive," meaning an intensive rehabilitation which includes a greater variety of exercises and sports related training. The aim of post-operative rehabilitation after ACL reconstruction is to restore normal joint motion and strength, and lower extremity performance reaching pre-injury levels without producing excessive stress and strain on graft during healing and also to prevent reinjury.[1]

Aim of the Study

1. The aim of our study is to assess the outcome of accelerated rehabilitation post-ACL reconstruction
2. A rehabilitation program for a duration of 6 months is sufficient when compared to 9 months
3. Role of KT 1000 arthrometer in the diagnosis of ACL tears.

MATERIALS AND METHODS

106 arthroscopic ACL reconstructions using quadrupled semitendinosis and gracilis grafts were performed. Meniscal injuries if associated were treated by partial meniscectomy.

This prospective study was conducted over a period of 4-year (2011-2014) at Vydehi Institute of Medical Sciences and Research Center Bengaluru in the Department of Orthopaedics.

All patients were examined preoperatively in the outpatient by a senior orthopedic surgeon. Evaluation was done clinically and also using KT 1000 arthrometer. Magnetic resonance imaging was done for all patients before surgery.

Patients with unilateral ACL insufficiency, injury at least 1 month prior to surgery, instability during activities of daily living, associated with other ligament and meniscal injuries and no previous reconstruction of any of the ligaments were selected as the study population. Patients with bilateral insufficiency, associated fractures in same limb and those put on delayed rehabilitation protocol were excluded. Following surgery, patients were prescribed on an accelerated rehabilitation protocol designed at our institute (Table 1) from day 1. The rehabilitation was supervised by trained rehabilitation therapist in coordination with the surgeon. Follow-up was done at 3 weeks, at 6 months, and at 9 months using the Lysholm knee score,[2,3] and KT 1000 arthrometer.[4,5]

Lysholm score has both subjective and objective evaluation. The score carries maximum points for instability and pain. The maximum points are 100. Patients are graded

Table 1: The accelerated rehabilitation protocol designed and followed in our institute

Rehabilitation Modality	Week 1	Week 2	Week 3	Week 4-8	2-4 months	4 months	5 months	6 months
Active, active assisted and gentle passive ROM exercises	+							
Gait toe walking assisted with axillary crutches	+							
Isometric quadriceps:hamstrings: 1:2	+							
Gait, 50% weight bearing with axillary crutches		+						
Active and active assisted knee ROM exercises		+						
Isometric quadriceps:hamstrings: 1:2		+						
Straight leg rises		+						
Gait, 75% weight bearing with axillary crutches 7			+					
Active and active assisted knee ROM exercises			+					
isometric quadriceps:hamstrings: 1:27			+					
Straight leg rises 7			+					
Extension exercises			+					
Full weight bearing gait				+				
Active, active assisted knee ROM				+				
Hamstring and quadriceps strengthening				+				
Quarter squats				+				
Custom knee brace				+				
Stationary bike				+				
Cycling					+			
Jogging					+			
Swimming					+			
Trampolines					+			
Proprioception exercises					+			
Sports specific skills						+	+	+
Continue hamstrings and quadriceps strengthening						+	+	+
Continue proprioception exercises						+	+	+

ROM: Range of motion

preoperatively and postoperatively as excellent, good, fair, and poor.

Scores:
81-100 - Excellent
71-80 - Good
61-70 - Fair
<60 poor (Table 2)

Observations

Out of 106 patients, who were selected, 96 (91%) were males and 10 (9%) were females. The commonest mode of injury was road traffic accident 43 (41%); this may be due to increased incidence of two wheeler accidents. This was followed by nonsports twisting injury in second place 41 (39%); we found out that majority 61% of the patients were in age group of 21-30 years. Of the 106 patients who were studied, out of which males were 96 (91%) and females were 10 (9%).

Table 2: Lysholm knee scores

Limp (5 points)	
None	5
Slight or periodic	3
Severe/constant	0
Support (5 points)	
None	5
Cane/crutch needed	3
Unable to bear weight	0
Locking (15 points)	
None	15
Catching	10
Occasional	6
Frequently	2
Currently locked	0
Instability (25 points)	
Never gives way	25
Rarely with sports	20
Often with sports	15
Sometimes with ADL's	10
Often during ADL's	5
Every step	0
Pain (25 points)	
None	25
Slight or periodic	20
Severe/constant	15
Marked walking >2 km	10
Marked walking <2 km	5
Constant	0
Swelling (10 points)	
None	10
After sports	3
After daily activities	2
Constant	0
Stairs (10 points)	
No problem	10
Slight problem	6
One step at a time	2
Impossible	0
Squatting (5 points)	
No problem	5
Slight problem	4
Not beyond 90°	2
Impossible	0

RESULTS

The mean pre-operative Lysholm score was 55.09. Postoperatively while on accelerated rehabilitation program the Lysholm scores were 69.73 at 3 weeks, 89.13 at 6 months and 89.19 at 9 months (Figure 1). In our pre-operative evaluation mean KT 1000 arthrometer score was 10.53 and post-operative at 6 months was 3.49. At 9 months, 105 patients had excellent results, whereas 1 patient had a good result.

DISCUSSION

The aim of rehabilitation the following ACL reconstruction is to enable the patient to get back to pre-injury levels without having the risk of reinjury.

In the present study, we found out that majority (65 patients and 61%) of the patients were in age group of 21-30 years. This shows that ACL injuries are common in the highly active age group. Thus, it becomes priority to restore them to pre-injury levels as early as possible.

All the patients were screened in the outpatient department clinically and using KT 1000 knee arthrometer. A difference of 4 mm on KT 1000 was considered significant when compared to the opposite knee. Our study indicated a tear in all the 106 patients (100%). In a study conducted by Bach *et al.*, KT 1000 is 95% sensitive in detecting ACL injuries.[6]

KT 1000 values of pre-operative and post-operative were compared in paired *t*-test which showed *t* value (96.73 df = 207) and *P* value (2.8×10^{-17}). This shows that there is a significant improvement in the outcome of the patients postoperatively in patients who have

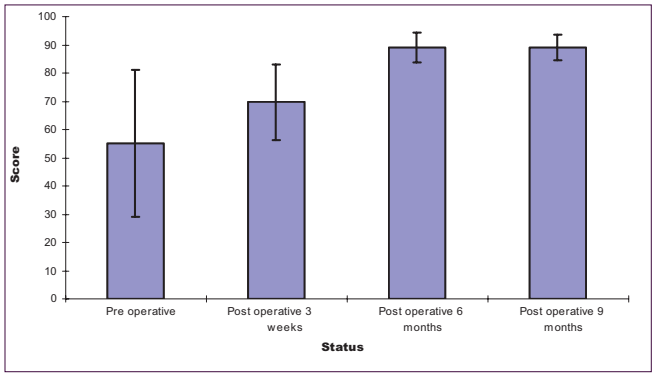

Figure 1: Mean lysholm scores

Table 3: Statistical Analysis

Lysholm score	Mean±SD	a and b	b and c	c and d	a and d
Pre-operative (a)	55.09±13.07				
3 Weeks post-operative (b)	69.73±6.74				
6 months post-operative (c)	89.13±2.68				
9 months post-operative (d)	89.19±2.26				
t-value	-	10.24	27.56	0.17	26.46
P-value	-	3.53×10^{-19}	9.7×10^{-58}	0.8681	9.35×10^{-50}
Statistical significance	-	Very highly significant	Very highly significant	Not significant	Very highly significant

SD: Standard deviation

undergone ACL reconstruction followed by an accelerated rehabilitation program. There is no statistically significant difference at the end of 6 months and at 9 months In KT 1000 arthrometer readings.

At 6 months the mean Lysholm score was 89.3, shows that the functional recovery of the operated and rehabilitated (accelerated) knee is excellent, which is comparable to the study of Shelbourne *et al.*, who showed that a score which is 85% of the normal knee is sufficient to get the patient back into pre-operative activity level.[7,8]

Statistical analysis was done using the pared *t*-test which showed the following (Table 3).

There is no statistically significant difference at end of 6 months and at 9 months. This is comparable with the findings of Shelbourne and Nitz,[9] Marcacci *et al.*,[10] and Freedman *et al.*[11] This indicates that only 6 months of accelerated rehabilitation protocol is sufficient.

In this study, 57 (48%) of the patients had associated meniscal injuries. The outcome in rehabilitation in them was no different from the patients who did not have meniscal injuries at end of 6 months. This is comparable to the study done by Barber and Click,[12] and Bellabarba *et al.*[13] In their study Barber *et al.*, followed up their patients for 2 years and found out that retear of meniscus was only 8-13% (development of pain and disability). None of our patients developed any retear during the course of rehabilitation.

In our rehabilitation program, patients were started on partial weight bearing on post-operative day 1 with weekly increments in weight bearing until patient started unaided gait at end of 3 weeks postoperatively. At end of 3 weeks, patients were allowed only normal walking. None of the patients complained of any instability. This is comparable to the study conducted by Tyler *et al.*[14] The advantage of early and incremental weight bearing is that patient is able to get back to day to day activities in a shorter time frame and simultaneously the graft in not subjected to strain.

Patients on accelerated rehabilitation regain lower limb muscle strength earlier when compared to delayed rehabilitation. Early recovery of muscle strength gives additional stability and help in returning to sporting activities at a faster rate compared to delayed rehabilitation without causing stress on the graft.[15]

In the rehabilitation protocol, we introduced proprioceptive exercises at 8 weeks, which helps in improving the nervous system's ability to generate a fast and optimal muscle contraction, enhance coordination and balance and to relearn movement patterns and skills. The importance of neuromuscular training has been demonstrated in prospective controlled studies where the incidences of ACL injuries were significantly lower in athletes who participated in proprioceptive training, as described by Fitzgerald,[16] and Zätterström *et al.*[17]

CONCLUSION

Accelerated rehabilitation protocol enables the patient to functionally recover a faster to pre-injury levels. A rehabilitation protocol for 6 months is sufficient in enabling a patient to get back to pre-injury levels. Functional outcome is the same with or without associated meniscal injuries. KT 1000 knee arthrometer plays a vital role in diagnosing ACL injuries and can be used to compare pre-operative and post-operative ligament status.

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Original Article

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Clot Retention - A Simple New Method of Evacuation with Out Toomey's or Ellick's: A Clinical Study

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Abstract

Background: The purpose of this clinical study was to assess whether our new method of clot evacuation is useful and better compared to conventional methods clot retention in the urinary bladder is a most common problem in surgical and non-surgical cases. Based our experience of 122 cases managed in 26 years. We discuss some guide lines which make this a safer and easier to perform.

Materials and Methods: During the period of June 1990 to June 2015, 122 cases of clot retention were treated. The non-surgical causes are upper tract bleeding, drug-induced bleeding, post-traumatic bleeding, and hemato-chyluria. The Surgical causes are the most common is post transurethral resection of the prostate bleeding.

Results: On reviewing the cases 115 males and 7 cases for females, it was found this method very simply and does not require any evacuator or syringe. This method easily adoptable and acceptable and no training are required.

Conclusion: Clot retention in the urinary bladder is the most common problem in surgical and non-surgical cases. Our technique of simple Venky's Suction and Nelton's catheter will help without any extra expenditure.

Key words: Clot evacuation, Clot retention, Hemorrhage, Prostate

INTRODUCTION

Hematuria is the most common post-operative unavoidable complication after transurethral surgery on the prostate and carcinoma bladder. Most men who have undergone such procedures have hematuria and clot formation in the post-operative period or on discharge from hospital are at risk of clot retention is a well-known problem.[1] We could find no previous reports on studies of methods for evacuation of formed clots new or old. We have not included the investigations for the duration of gross hematuria after these operations. Similarly, despite the frequent mention of clot retention in this reports.[2-5] None specifically mentioned methods of evacuation of this complication. We, therefore, present our simplified method of clot evacuation.

Clot retention in the urinary bladder is the most common problem in surgical and non-surgical cases all over the world. There are a lot of methods described, but the method which we adopt is simple and easy to follow.

MATERIALS AND METHODS

During the period of June 1990 to June 2015, 122 cases of clot retention were treated. The non-surgical causes are upper tract bleeding, drug-induced bleeding, post-traumatic bleeding, and hemato-chyluria. The surgical causes are the most common is post transurethral resection of the prostate (TURP) bleeding.

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Operative Technique

The patients were kept in lithotomy position in operation theatre (Figures 1 and 2). Commonly local and occasionally spinal and rarely general anesthesia was used.

24F resectoscope sheath and occasionally 21F urethrotome sheath were used. Regularly, Toomey Syringe or Ellick Evacuator is used to remove/evacuate the clots from the bladder. Sterile water used for bladder wash and clot evacuation (Figures 3 and 4).

We have devised using simple Venky's suction apparatus with medium pressure and 16F nelatons catheter with tip cut up to 1 cm is attached to the suction pipe, and it is introduced through 24F resectoscope sheath, and it simply evacuates the clots without any injury to the bladder and without causing any trauma. Per abdominally, we can palpate/feel the bladder being emptied. We can do a cystoscopy to verify for any residual clots. This is a very simple method and the old and hard clots also can be removed.

The individual cases of etiology can be managed accordingly.

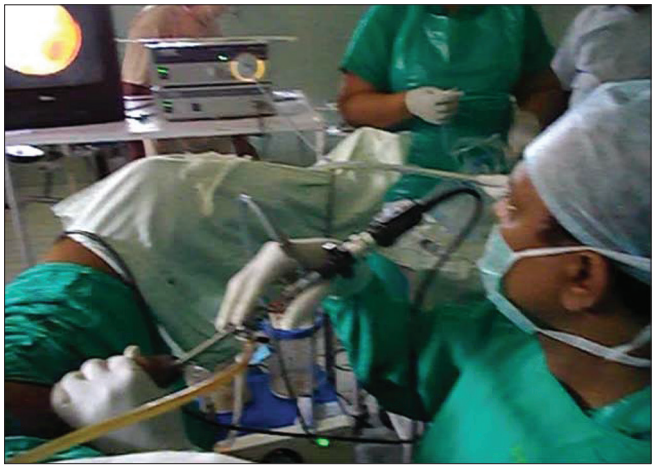


Figure 1: Video cystoscope in position

Figure 2: Nel cath with suction tube *in situ*

RESULTS

The main result is equal in all cases, i.e., evacuation is complete in all cases. The incident of cases of clot retention in post TURP are day 1 are 6 cases, 2nd day 88, 3rd day 7 cases, 7th day 5 cases, and at 1 month one case. In transurethral resection of a bladder tumor, 11 cases had clot retention in day 1. Others include hemoto-chyluria, upper tract bleeding, and post radiotherapy carcinoma cervix (Table 1 and Graph 1).

Table 1: Presentation of clot retention

Number of days	TURP	TURBT	Others
Day 1	6	11	4
Day 2	88		
Day 3	7		
Day 7	5		
Day 30	1		

TURP: Transurethral resection of the prostate, TURBT: Transurethral resection of a bladder tumor

Figure 3: Clots in suction tube

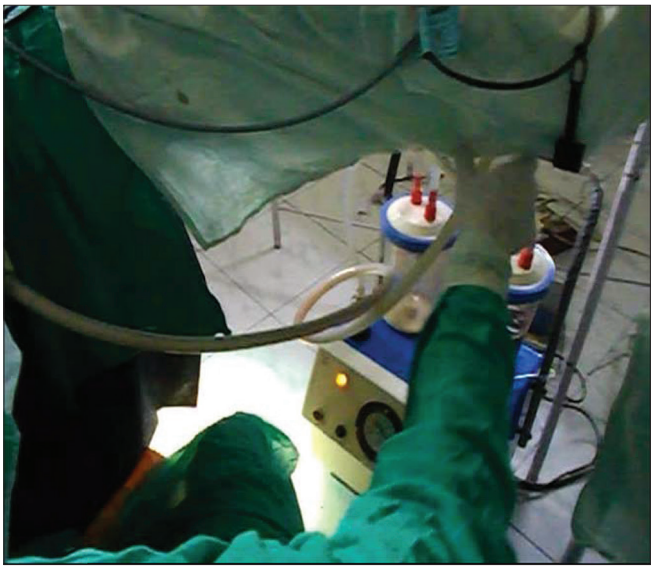
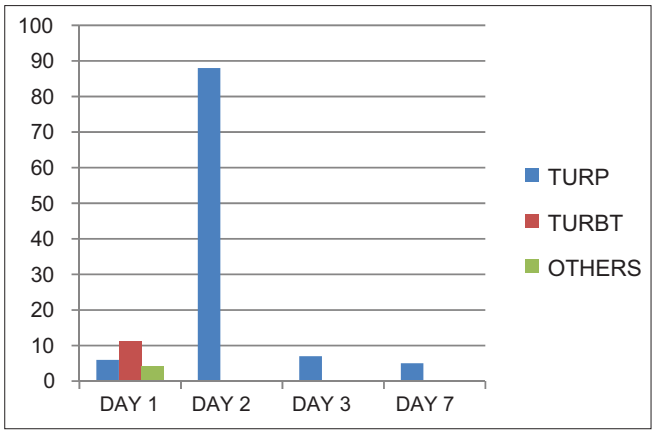


Figure 4: Clots being collected in suction apparatus



Graph 1: Incidence of clot retention day

DISCUSSION

Using Toomey's glass or plastic syringe requires lot of stress and power to remove clots. By using Ellick's evacuator sometimes, it may be difficult to evacuate old clots.

Post-operative bleeding can be secondary to inadequate control of bleeding during the intra operative period it can also occur with increased activity of the patient (i.e., straining with a bowel movement). Therefore, we recommend a stool softener to reduce straining should the patient continue to bleed, we recommend returning into the operating room were clots can be was from the bladder. With the removal of the clot, usually the site of bleeding is not apparent. The patient usually does well with complete evacuation of the clots in the bladder and prostatic fossa.[6-8] Occasionally, a patient will have persistent bleeding, even though cystoscopy was done, no bleeding point was found, and no blood dyscrasia was identified. Significantly higher intra operative bleeding rates were associated with glands weighing more than 45 g and resection times longer than 90 min.[9-12]

Clot retention in the urinary bladder is the most common problem in surgical and nonsurgical cases. Our technique of simple Venky's Suction and Nelton's catheter will help without any extra expenditure. It does not require any special expertise to learn this method.

CONCLUSION

Clot retention once occurs has to be dealt on an emergency basis. Most of the time blood transfusion is required. Each individual case has to be handled according to its severity. Compared to other methods this method is ready to use. The available armamentarium is sufficient to handle this emergency condition in the operation theater.

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Original Article

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Post-Shunt Gait Improvement Correlates with Increased Cerebrospinal Fluid Peak Velocity in Normal Pressure Hydrocephalus: A Retrospective Observational Phase-Contrast Magnetic Resonance Imaging Study

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Abstract

Background: The relationship between peak velocity (PV) of cerebrospinal fluid (CSF) through the cerebral aqueduct and gait performance is not well characterized in normal pressure hydrocephalus (NPH) patients who undergo ventriculoperitoneal shunting (VPS). Therefore, our goal was to examine this relationship and test the hypothesis that aqueductal CSF PV in an NPH group is correlated with gait function pre- to post-shunt.

Methods: Seven patients with idiopathic NPH who demonstrated gait improvement following large volume spinal tap or lumbar drain procedure and subsequent VPS were retrospectively studied. Patients underwent magnetic resonance imaging (MRI) and gait evaluation (functional ambulation performance [FAP] and gait time [GT] tests) before and after VPS. Aqueductal cross-sectional area (ACSA), PV, and total ventricular volume were obtained from semi-automatic segmentation of phase-contrast and 3D, T_1-weighted MRIs while FAP and GT were obtained from neurological assessment. All mean changes pre- to post-VPS were tested using paired-sample *t*-tests, and all correlations using Pearson's correlation coefficient.

Results: Mean PV increased 25% pre- to post-VPS (mean ± standard deviation: 6.9 ± 3.6 to 8.3 ± 3.8 cm/s, $P < 0.01$); ACSA decreased 24% (6.5 ± 2.6 to 4.8 ± 1.9 mm^2, $P < 0.05$), FAP increased 14% (73.3 ± 15.9 to 82.1 ± 13.3, $P = 0.05$); total ventricular volume decreased 11% (140 ± 27 to 124 ± 25 cm^3, $P < 0.01$). GT decreased 14% (44.5 ± 70.8 to 27.3 ± 30.6 ms, $P = 0.3$), but the change was not statistically significant. Mean PV increase strongly correlated with ACSA decrease ($R = 0.90$, $P < 0.01$), FAP increase ($R = 0.76$, $P < 0.05$), and GT decrease ($R = 0.91$, $P < 0.01$).

Conclusions: The observed relationships between PV and gait metrics, and PV and ACSA independently suggest a complex and dynamic biophysical mechanism common to NPH patients undergoing shunt placement. A larger prospective study with longitudinal measures is warranted.

Key words: Cerebrospinal fluid, Gait, Neurological disorders, Normal pressure hydrocephalus, Shunt, Velocity

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INTRODUCTION

It is estimated that 1-10% of all elderly and up to 6% of nursing home residents have normal pressure hydrocephalus (NPH).[1] Our own imaging experience suggests a much larger prevalence of radiologic communicating hydrocephalus with or without the

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symptomatology of NPH. In addition, approximately 375,000 Americans with NPH are thought to be misdiagnosed with dementia or Parkinson's disease.[2] Therefore, diagnosis of idiopathic NPH and, in particular, the identification of potential shunt responders remains a challenge. An invasive procedure, that has withstood the test of time, is lumbar puncture (LP) with high volume cerebrospinal fluid (CSF) drainage with gait testing performed before and after LP. Gait improvement after high volume LP identifies patients who are likely to respond to ventricular shunting.

Successful treatment of NPH can ameliorate symptoms in up to 80%[3-8] of shunted patients and over 90% of patients at our institution (unpublished data). Identifying non-invasive means of diagnosing NPH and NPH shunt candidates is a highly desirable objective.

Phase-contrast magnetic resonance imaging (MRI) metrics, in particular, the peak velocity (PV) of CSF flow, characterizes a subset but not all NPH patients, and prior studies have shown higher group PV in NPH compared with healthy controls.[9,10] Furthermore, Sharma *et al.*,[11] recently demonstrated the utility of measuring PV both before and after lumbar CSF drainage as a way to determine NPH patients likely to improve following ventricular shunt placement.

Bradley *et al.*,[12] demonstrated that pre-operative CSF stroke volume through the aqueduct of 42 uL or more was associated with shunt response in all patients (n = 12). PV was not reported to be a useful measure.

To the best of our knowledge, no phase-contrast MRI study has yet determined the association of changes in aqueductal PV with changes in symptom severity from pre- to post-shunt. We observed aqueductal flow changes through the aqueduct prior to and as a result of the ventricular shunt and related these changes to gait measures. We chose PV for flow quantification since this measure, unlike other flow parameters, varies minimally across observers, as PV always occurs at or near the center of flow in a tubular structure.

Since gait impairment is the principal symptom in many NPH patients[13] and also the clinical parameter most likely to improve after shunt,[14,15] gait function measures were used as markers of disease severity and for monitoring symptom improvement. Consequently, our goal was: (a) To establish the relationship, if any exists, between change in aqueductal PV and change in gait performance pre- to post-shunt, and (b) to test the hypothesis that aqueductal PV is correlated with gait function.

METHODS

Subjects

This retrospective, anonymized, single-center, health insurance portability, and accountability act-compliant study was exempt from Institutional Review Board approval. We reviewed patients who were referred to New York University 's (NYU) adult hydrocephalus evaluation program for symptoms of gait impairment (irrespective of the presence of cognitive or urologic dysfunction) and enlarged ventricles and who underwent ventriculoperitoneal shunting (VPS) between January of 2012 and December of 2013. All patients were examined by a board-certified study neurologist (25 years of experience) who made the initial diagnosis of NPH, and frequently followed up on patients through the post-shunt time period monitoring for disease symptoms and shunt failure. All patients underwent a standardized shunt surgery. The clinical diagnosis of probable NPH was made on the basis of enlarged ventricles, a characteristic dyspraxic gait disorder, marked improvement to either high volume CSF LP and/or continuous lumbar drainage, and exclusion of other confounding diagnoses such as Parkinson's disease, cerebellar dysfunction, cerebrovascular disease, myelopathy, and/or metabolic disease known to cause gait problems. We reviewed retrospectively seven patients (six men/one woman) who: (a) Had available pre- and post-surgical high-resolution (1 mm) isotropic, 3D T_1-weighted, magnetization-prepared rapid acquisition gradient echo (MP-RAGE) MRI needed for ventricular segmentation, and (b) had pre- and post-shunt phase-contrast MRI scans. Age at pre-shunt MRI was 74.4 ± 3.5 (mean ± standard deviation), range: 68.8-78.6 years. Age at post-shunt MRI was 75.1 ± 3.4, range: 69.0-79.0 years.

Clinical Evaluation

Gait impairment and its subsequent improvement following ventricular shunting were assessed with two gait metrics: (i) The functional ambulation performance (FAP) score and (ii) gait time (GT), defined as the time to walk ~9 m (30 ft) and return. The FAP score is a well-validated, quantitative composite gait measure based on step length, symmetry, velocity, and ranges from 95 to 100 in healthy adults.[16] It was determined using the GaitRite System (CIR Systems, Inc., Havertown, Pennsylvania, USA).[17] Both GT and FAP measures consist of six individual trials that are averaged together.

Cognitive status and urinary incontinence were used for clinical characterization by the Neurologist. Cognitive function was evaluated using the Mini Mental State Examination and the global deterioration scale.[18] The global deterioration scale score pre- and post-shunt was identical

for each patient, with a mean of 2.9 (range: 2-6). Mean Mini Mental State Examination score was 25.4 pre-shunt (range: 15-30) and 26.6 post-shunt (range: 17-30). Urinary incontinence was queried by means of a questionnaire administered at initial clinical assessment and scored on a scale from 0 (no incontinence) to 9 (three or more incontinent episodes per day). Mean urinary incontinence score for the patients was 4.1 pre-shunt (range: 0-9) and 3.0 post-shunt (range: 0-7). Patients were clinically evaluated at the time of imaging and immediately prior to shunt placement, with no reported significant difference in impairment based on NPH symptomatology.

MR Imaging Data Acquisition

Patient logs of the NYU adult hydrocephalus service were reviewed to identify all patients for whom pre- and post-shunt phase-contrast MRIs were acquired and who were studied and followed up by a neurologist. Subject MRI scans were anonymized and transferred off-line for in-house processing at NYU School of Medicine. Pre-shunt MRI was performed 8-218 days before shunt (median=50 days) and 55-488 days following shunt (median=104 days).

MRI Image Evaluation

All subjects had T_1-weighted brain MRI acquired using the 3D MP-RAGE sequence on either a Siemens 1.5 or 3T unit (Avanto, TrioTim, or Skyra; Siemens AG, Erlangen, Germany). The TR ranged from 1590 to 2200 ms, TE ranged from 2.26 to 2.48 ms, field-of-view: 256 mm, matrix size: 256 × 256, slice thickness: 1 mm. The bandwidth was set to 250 or 260 Hz across scans. PV in the aqueduct was obtained using a phase-contrast method, as described elsewhere.[19,20] Prospective cardiac gating used was either finger plethysmography or electrocardiogram leads for a range of 17-42 segments of acquisition. The TR ranged from 22.25 to 28.6 ms, TE ranged from 6.08 to 8.87 ms, field-of-view ranged from 180 to 230 mm, matrix size: 256 × 256, slice thickness: 5 mm. The V_{enc} was set from −20 cm/s to 20 cm/s. Bandwidth was set to 130 or 201 Hz across scans. The local plane of acquisition for all subjects was midway through the aqueduct of Sylvius at 90° transverse orientation, as shown in Figure 1.

Orientation of plane of section for flow measurements. Mid-sagittal T_2-weighted MRI with flow compensation off. Note the solid, white line indicates axial position of slice used for CSF PV measurements in the aqueduct of Sylvius.

Image Analysis

To approximate the contours of the cerebral aqueduct and to calculate the PV, a region-of-interest (ROI) was manually placed for each phase of the study using circle cardiovascular magnetic resonance (CMR) 42 software (Circle Cardiovascular Imaging, Calgary, Alberta, Canada), which approximates the dimensions of the cerebral aqueduct to optimally calculate the cross-sectional area of the ROI as shown in Figure 2a and b.

Cerebral aqueduct for flow measurements (a): Anatomical phase-contrast MR image at 90° transverse orientation relative to the plane shown in Figure 1. Right (b): A ROI was placed using CMR 42 software on the aqueduct to best match the contours of the structure. Note the bright CSF suggests craniocaudal flow.

The cross-sectional area of each ROI is averaged across all phase images of the acquisition to yield an average aqueductal cross-sectional area (ACSA). Given that prospective gating neglects, a portion of the cardiac cycle and plethysmography gating omits a different portion altogether than EKG gating, the PV graph for each phase was inspected to ensure the PV was not obtained at the first or last phase for each patient's scan as this may have produced an erroneous result. From inspection, there was no apparent difference in the flow waveform when comparing a patient's pre-shunt scan with his/her post-

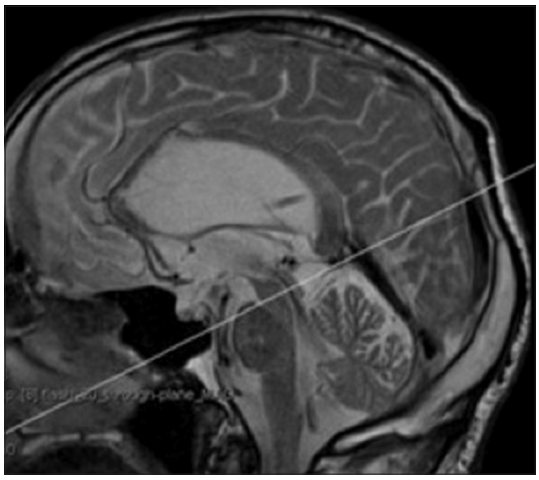

Figure 1: Plane of flow measurement acquisition

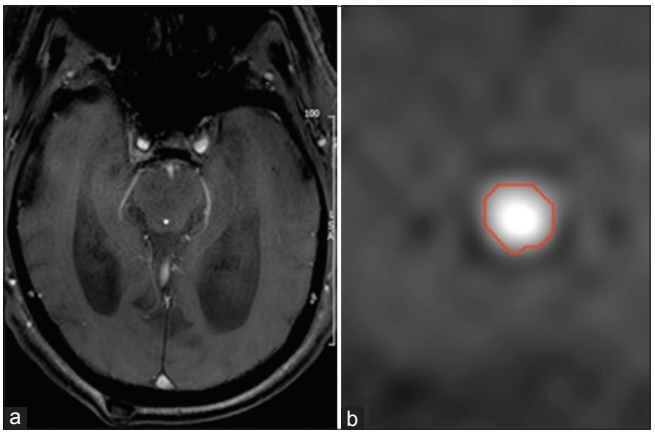

Figure 2: (a and b) Peak velocity measurements using cardiovascular magnetic resonance 42 software

shunt scan. This suggests a consistent craniocaudal flow direction and amplitude throughout all phase acquisitions. Total ventricular volume was generated in three steps using fire voxel:[21] (a) Bridge burner algorithm was used to segment the whole brain excluding CSF;[21] (b) morphologic closure of the brain mask was performed to include the ventricular spaces; (c) 3D set difference of (a) subtracted from (b) was taken as the ventricular volume.

Retrospective cardiac gating was not available in this group of patients, and stroke volumes were not obtained. Our current NPH protocol includes retrospective cardiac gating and stroke volume acquisition.

Statistical Analyses

The temporal change in each gait impairment metric and PV was computed for each subject as the "pre-" minus the "post-" surgery level so that a positive change reflects a decline over time. Paired sample *t*-tests were used to assess the temporal change in each metric pre- to post- shunt. All correlations were tested using Pearson's correlation coefficient. Significance was set at $P < 0.05$ and Minitab version 14 (Minitab Inc., State College, Pennsylvania, USA) was used for all analyses.

RESULTS

There were no significant differences from pre- to post-shunt in dementia scores or urinary incontinence. In terms of ait impairment, metrics for all seven patients before and after shunt are compiled in Table 1. Five out of seven patients had quantifiable gait improvement following shunt while two patients had stable to decreased gait scores following shunt.

Mean FAP increased 14% ($P = 0.05$), while mean GT decreased 14% ($P = 0.3$), but this change was not statistically significant. There was no significant association of GT or FAP score with age ($R = 0.03$, $P = 0.95$; $R = 0.12$, $P = 0.80$, respectively).

Mean PV increased 25% ($P < 0.01$).

Relationship between Gait Impairment and Flow Velocity

PV values for all seven subjects prior to and after ventricular shunting are provided in Table 2.

There was no significant association of pre-shunt PV with improvement in FAP score ($R = 0.25$, $P = 0.59$). In addition, there was no significant association of pre-shunt PV with % change in GT ($R = 0.30$, $P = 0.51$). However, % change in either FAP score or GT with absolute PV difference (pre- to post-shunt) revealed a significant association ($R = 0.76$, $P < 0.05$; $R = 0.91$, $P < 0.01$, respectively), as shown in Figure 3a and b.

Relationship between pre- to post-shunt changes in PV and gait metrics (a): Pre- to post-shunt percent (%) change in GT versus absolute difference in PV (post-shunt minus pre-shunt values) for each patient ("•"). Bottom (b): Pre- to post-shunt % change in FAP score versus absolute difference in PV for each patient ("•").

ACSA and Total Ventricular Volume

Pre- and post-shunt ACSA and ventricular volume are provided for each subject in Table 3.

Table 1: Quantitative gait metrics for each normal pressure hydrocephalus patient, pre- and post-shunt

Patient	Pre-shunt FAP	Post-shunt FAP	Pre-shunt GT (s)	Post-shunt GT (s)
1	45.0	54.5	204.4	96.0
2	64.1	89.3	30.4	17.6
3	80.8	89.7	16.1	14.7
4	75.8	75.3	20.5	23.8
5	83.7	89.7	10.5	9.6
6	69.0	84.8	17.1	16.1
7	94.5	91.2	12.8	13.6
Mean	73.3	82.1	44.5	27.3
SD	15.9	13.3	70.8	30.6

SD: Standard deviation, FAP: Functional ambulation performance, GT: Gait time

Table 2: CSF PV for each patient, pre- and post-shunt

Patient	Pre-shunt PV (cm/s)	Post-shunt PV (cm/s)
1	11.09	13.22
2	4.24	6.52
3	6.81	8.25
4	6.27	6.37
5	4.9	6.53
6	12.27	13.54
7	2.56	3.56
Mean	6.9	8.3
SD	3.6	3.8

SD: Standard deviation, PV: Peak velocity, CSF: Cerebrospinal fluid

Table 3: Pre- and post-shunt ACSA and ventricular volume for each normal pressure hydrocephalus patient numbered 1 through 7

Patient	Pre-shunt		Post-shunt	
	ACSA (mm^2)	Ventricular volume (mL)	ACSA (mm^2)	Ventricular volume (mL)
1	5.65	161	4.62	142
2	11.46	121	6.15	108
3	5.39	166	3.40	134
4	8.41	152	8.28	147
5	5.41	95	3.71	91
6	4.97	163	4.49	149
7	3.95	122	2.89	95
Mean	6.5	140	4.8	124
SD	2.6	27	1.9	25

SD: Standard deviation, ACSA: Aqueductal cross-sectional area

Mean ACSA decreased 24% ($P< 0.05$), while the mean ventricular volume decreased 11% ($P < 0.01$). No significant association was found between ACSA and ventricular volume. No significant association was found between relative % change in ventricular volume and ACSA ($R = 0.32$, $P = 0.48$); neither was an association found between absolute difference in ventricular volume and ACSA ($R = 0.05$, $P = 0.92$).

Relationship between PV and ACSA and Total Ventricular Volume

There was a significant association between % change in PV and % change in ACSA ($R = 0.90$, $P < 0.01$), as shown in Figure 4.

Pre- to post-shunt increase in PV (given as percent [%]) versus decrease in ACSA (given as %) for each patient ("•").

However, no association was found between % change in PV and % change in ventricular volume ($R = 0.38$, $P = 0.40$).

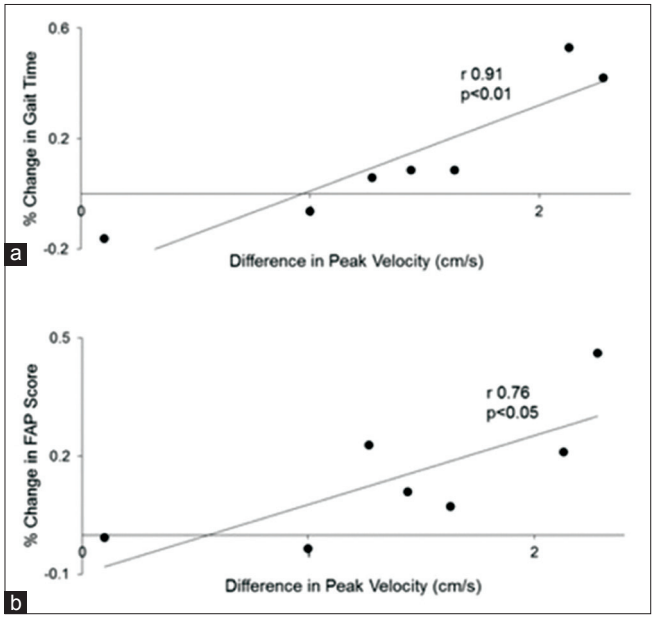

Figure 3: (a and b) Changes in cerebrospinal fluid flow versus changes in gait metrics

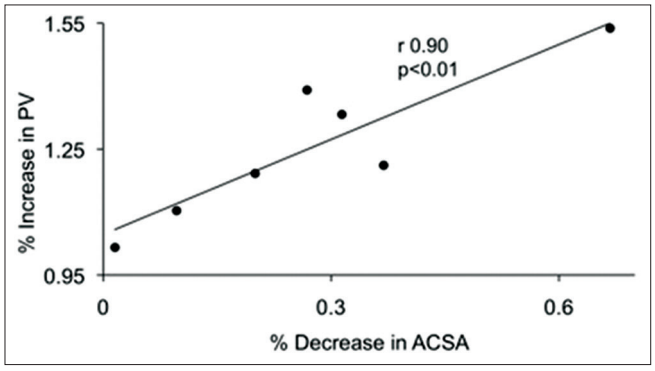

Figure 4: Relationship between cerebrospinal fluid flow and aqueductal caliber

DISCUSSION

Phase-contrast CSF flow studies have been increasingly used as a tool to study patients with NPH. However, the dynamics of CSF flow at the cerebral aqueduct in patients with NPH, and how they relate to clinical symptoms, are still not well-understood. Current research is neither consistent nor abundant in terms of what the flow patterns are for NPH shunt-responders versus non-responders and how these values change following VPS. The results from our study cohort suggest a strong correlation exists between PV and gait metrics following VPS.

At first the finding that NPH patients post shunt demonstrate higher PV may appear counter-intuitive, however, only a few studies in the literature have investigated the definitive hydrodynamic treatment response after VPS, and all differ for various reasons from our current study, especially with regard to aqueductal PV in patients with idiopathic NPH, i.e. the development of NPH without prior pathological or traumatic insult.

Abbey *et al.*,[22] observed a decrease in PV from pre-to post-shunt in a group (N=10) with communicating hydrocephalus. Differences from our study include: (a) younger age group 17 to 50 years of age 50% of whom were under 30 years in the Abbey study and 68.8-78.6 years in our study; (b) the Abbey patient sample consists of 8 patients who developed hydrocephalus secondary to another event and 2 cases of idiopathic NPH; all our cases of NPH are idiopathic.

In secondary NPH the primary disease typically meningitis or trauma may result in cerebritis, infarcts, post-contusional gliosis, and atrophy as well as adhesions in the subarachnoid spaces, including the aqueduct all of which may have an effect on CSF dynamics and aqueductal flow.

Scans were performed 2-20 days post shunt and all scans were performed on a 1.5T scanner. In our study, the post shunt studies were performed 104 days (median value) after shunt. It is unknown whether post shunt PV is dependent on these factors: Patient age, the cause of NPH, secondary versus idiopathic, field strength of the MRI scanner and time to post shunt MRI.

A study by Kim *et al.*,[23] also demonstrated that PV "decreased somewhat" (significance not indicated) after shunt in 11 cases of NPH, with an average age of 50 years and age range of 20-67 years (pre-operative 6.71 ± 2.84 cm/s and post-operative 5.16 ± 3.84 cm/s). It is not stated whether the NPH was idiopathic or secondary. This age range is younger than the age in our sample and is distinctly younger than typically seen in patients

with idiopathic NPH. The younger age in the Kim study suggests the inclusion of secondary NPH patients.

In summary, both of the above earlier studies are in younger patient populations and are in large part studies of secondary NPH. In addition, symptom improvement was only qualitatively evaluated, while in our study we found not only a quantitative increase in PV but also that this increase is linked with a quantifiable degree of symptom improvement.

Sharma *et al.,*[11] in a pre-operative only MRI PV study before and immediately following high volume CSF LP, demonstrated, that patients with >2 cm/s decreased PV following 50 cm^3 lumbar CSF drainage had symptomatic improvement the following shunt. This study of alterations in the aqueductal hydrodynamics immediately after large volume CSF drainage may not reflect aqueductal hydrodynamics several months after permanent ventricular shunt placement. The effects on PV of the temporal progression of the disease, and alterations in CSF hydrodynamics over time in response to VPS are unknown at this time.

Prior studies[24-27] suggest that pre-shunt elevated flow measures in NPH, may not be reliable as a surrogate marker for response to spinal tap or for quantifying disease severity. Although Algin *et al.,*[10] found higher flow values for NPH patients, there was no correlation between these values and patient shunt response. Moreover, Dixon *et al.,*[27] were unable to use pre-shunt CSF flow rates as a means to predict shunt-responders. Furthermore, this group found mean aqueductal CSF flow was significantly increased in patients with negative responses to high-volume LP compared with the mean flow in LP-responders. In our current study, as well, pre-operative PV did not correlate with shunt response.

We also found that the NPH patient group had significantly decreased ventricular volume following VPS. However. there was no significant relationship between ventricular volume change and change in gait metrics. This agrees with other studies that show significant clinical improvement can occur after shunt, even without a reduction in ventricular size.[28-30] Thus, although a clear reduction in ventricular size was observed in our patient group, consistent with previous studies,[28-30] there may not be a measurable association between ventricular size and patient symptomatology.

Admittedly, there are several limitations to our study. The first, we demonstrated our findings with a small number of patients and with retrospective clinical and radiographic data. Future work including longitudinal assessments will focus on increasing the sample size to prospectively, replicate and confirm that increased aqueductal PV correlates with improvement in gait metrics and to investigate the relationship of PV to stroke volume.

CONCLUSION

In conclusion, our study shows evidence that changes in CSF PV through the aqueduct is directly related to the degree of gait improvement. The study also suggests in conjunction with previous reports that aqueductal PV and hydrodynamics are complex and likely dynamic phenomena that may change over time. The results from our study help shed light on one aspect of the physiology of the disorder. Further study is warranted and, in particular, longitudinal studies to help determine the role of aqueductal PV and hydrodynamics in the diagnosis and management of this debilitating but treatable condition.

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Original Article

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Correlation of Pap Smear and Colposcopy in Relation to Histopathological Findings in Detection of Premalignant Lesions of Cervix in A Tertiary Care Centre

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Abstract

Objective: Correlation of papanicolaou (PAP) smear and colposcopy in the detection of premalignant lesions of cervix.

Materials and Methods: A prospective observational study was conducted in a tertiary care referral institute in 100 symptomatic, sexually active women of 20-65 years. PAP smears were performed by the conventional method and colposcopy was done for all 100 women who came with complaints of white discharge per vagina, intermenstrual, or postcoital bleeding, etc. Final correlation of the PAP smear and colposcopy were based on histopathology reports.

Results: In cytology and colposcopy-directed biopsy sensitivity is 65.38%, specificity is 95.83%. Positive predictive value 94.4%, negative predictive value 71.8% and accuracy are 80%.

Conclusion: In the present study, incidence of cervical intraepithelial neoplasia I (CIN I) was 28%, CIN II 11%, CIN III 4%, carcinoma *in situ* 2%, squamous cell carcinoma 5%, and adenocarcinoma 2%. This emphasizes the use of all 3 methods PAP cytology (conventional method), colposcopy, and histology is complementary to each other and helps to reduce false negative cases.

Key words: Adenocarcinoma, Colposcopy, Histopathology, Papanicolaou cytology, Squamous cell carcinoma

INTRODUCTION

According to the World Health Organization (WHO), cervical cancer is the second most common type of cancer among women's.[1] The main cause of cervical cancer is a sexually transmitted infection by human papillomaviruses.[2] The worldwide human papiloma virus prevalence in cervical cancer is 99.7%.[3] Cancer cervix has been considered preventable because it has a long pre-invasive state and availability of screening programs and treatment of pre-invasive lesion is effective.[1] It has been well-established that well-organized screening by conventional cytology has substantially reduced the incidence of morbidity and mortality from cervical cancer in developed countries.[1]

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In developed countries such as the USA, 85% of women had at least one papanicolaou (PAP) test through their lifetime, but this rate is only 5% in the developing countries.[4] The goal of screening of carcinoma of cervix is to diagnose and treat carcinoma cervix in early pre-invasive states make the disease ideal for screening procedures.[1] The PAP smear is a simple, safe, non-invasive and effective method for detection of precancerous and noncancerous changes in the cervix and vagina.[5] In 1925 Hinsellman 1st hypothesized visualization of cervical epithelium under the magnification. Colposcopy provides a unique method to study the benign and premalignant lesions.[5] It is a simple noninvasive procedure which helps in determining the

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location, size and extent of abnormal cervical lesions and serves for detecting the site for biopsies. Colposcopy is complementary to cytology.[6] Cytology (PAP smear) is the lab method while the colposcopy is the clinical method of detection.[6] The final diagnosis must be made on histopathological examination.[6] PAP smear were interpreted according to The New Bethesda System 2014.[7] Histopathological slides were interpreted according to the WHO classification 2003.[8]

The aim of this study was to find a correlation of PAP smear and colposcopy in detecting the premalignant lesions of the cervix.

MATERIALS AND METHODS

This prospective study was conducted in the Department of Pathology Pt. J. N. M. Medical College, Raipur, Chhattisgarh, India, and Dr. Bhim Rao Ambedkar Memorial Hospital, Raipur, Chhattisgarh, India, from 15th July 2014 to 15th June 2015 after taking approval from Institutional Ethical Committee.

The material of present study was collected from women who met the inclusion criteria and gave the consent for colposcopy and directed biopsy from the Department of Obstetrics and Gynecology, Dr. Bhim Rao Ambedkar Memorial Hospital, Raipur, Chhattisgarh, India.

Inclusion Criteria

- Sexually active women of age group of 20-65 years
- Abnormal vaginal discharge, abdominal pain, irregular menstrual bleeding, post-menopausal bleeding, postcoital bleeding, prolapse, and burning micturition.

Exclusion Criteria

- Women >65 years and <20 years, women with frank cancer, pregnant women, and post total hysterectomy patients
- Unsatisfactory smears for evaluation.

Written and informed consent was taken from all the patients after a brief explanation of the procedure. A careful history including demographic data like age, socioeconomic status, education, parity, age at marriage of the patient, was taken. General examination and systemic examination was done. Information is noted on pretested proforma.

Prepared PAP smear slides were received fixed in 95% ethyl alcohol and ether. All the women were subjected to colposcopy and cervical biopsy. Biopsy specimens were received in 10% formalin fixative. The prepared PAP smears slides were then stained according to the conventional PAP technique and examined under a light microscope. The cytological interpretation of the smears was made according to the Bethesda system 2014.

Colposcopy-directed biopsies were processed, histopathological slides prepared and stained with hematoxylin and eosin and examined under a light microscope. Biopsy results were categorized as chronic cervicitis, cervical intraepithelial neoplasia I (CIN I), CIN II, CIN III, carcinoma *in situ*, squamous cell carcinoma (SCC) and adenocarcinoma according to WHO.

Statistical analysis was carried out by for calculating sensitivity, specificity and positive and negative predictive value (NPV) of PAP smear, colposcopy, and histopathological examination.

RESULTS

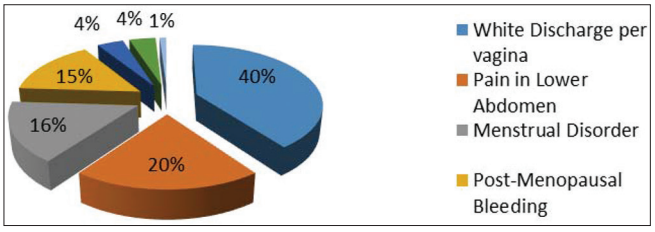
In the present study, women attending gynecology outpatient department had PAP smears were subjected to colposcopy and directed biopsy. The results of histopathology were compared and analyzed.

Total of 874 PAP smears were taken from 15th July 2014 to 15th June 2015, which is the time period of our study. Out of these 100 (11.4%) patients had abnormal PAP smear were interpreted. Colposcopy findings and colposcopic-directed biopsy were received from the Department of Obstetrics and Gynecology, and histopathological examination was done. The peak age group was between 41 and 50 years, 57% were menopausal cases, 93% women were from rural areas, and 20% were literate (Figure 1-6).

In Graph 1, it shows the most common presenting complaint was white discharge per vagina in 40% cases.

In Table 1, it shows the most common finding was acetowhite area in 43% cases under colposcopy.

In Graph 2, it shows that 64% PAP smears were interpreted as negative for intraepithelial lesion or malignancy (NILM).



Graph 1: Distribution of cases in relation to presenting complaint

Graph 3 depicts that out of 64 cases of NILM, 60 cases are of inflammatory smear, 2 are of trichomonas vaginalis, 1 of candida albicans and 1 of bacterial vaginosis.

In Table 2, it shows the most common histopathological finding was chronic cervicitis which accounts for 48% as compared to other findings.

In Table 3, it was seen that the most common biopsy result in inflammatory smear was chronic cervicitis which accounts for 46%.

Table 4 depicts the correlation of the PAP smear along with colposcopic finding out of which NILM accounted for 65%.

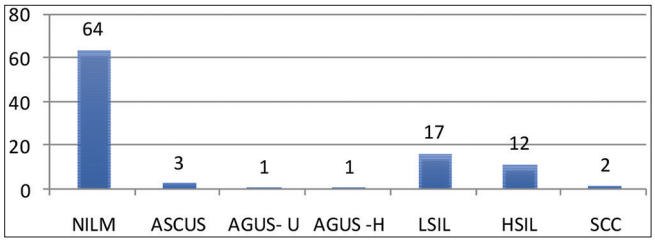
In Table 5, it was shown the correlation between histopathological findings with colposcopic finding.

Table 6 showed about the correlation between PAP smear and histopathological diagnosis in which positive accounted for 36% and negative for 64%.

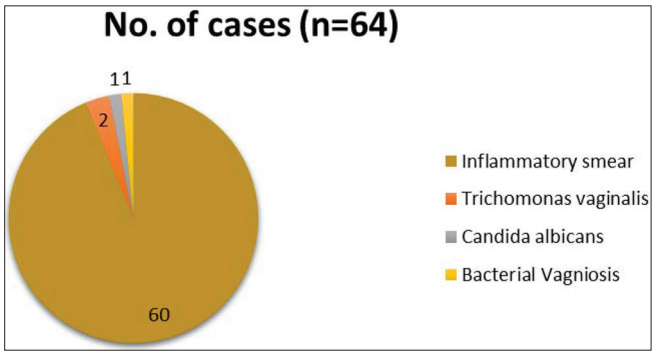
Table 7 depicts about sensitivity and specificity of PAP smears along with the positive predictive value (PPV), NPV and accuracy.

DISCUSSION

In the present study, the maximum number of cases were in the age group of 41-50 years (50%), similarly reported by Sharma *et al.*,[9] and by Algotar *et al.*[10] In study of Goyal *et al.*,[11] the mean age was 39.38 years.



Graph 2: Papanicolaou smear interpretation by the 2014 Bethesda system



Graph 3: Pattern of negative for intraepithelial lesion

Table 1: Distribution of cases according to colposcopic finding

Colposcopic finding	Number of cases	Percentage
Normal	27	27
Acetowhite area	43	43
Punctation	16	16
Mosaic pattern	14	14
Total	100	

Table 2: Histopathological findings

Histopathological findings	Number of cases	Percentage
Chronic cervicitis	48	48
CIN I	28	28
CIN II	11	11
CIN III	4	4
CIS	2	2
SCC	5	5
Adenocarcinoma	2	2
Total	100	100

CIN: Cervical intraepithelial neoplasia, CIS: Carcinoma *in situ*, SCC: Squamous cell carcinoma

Table 3: Correlation of PAP smear and histopathological diagnosis

PAP smear	Histopathological finding							
	CC	CIN I	CIN II	CIN III	CIS	SCC	Adenocarcinoma	Total
NILM	46	11	4	1		2		64
ASCUS		3						3
LSIL	1	14	2					17
HSIL	1		5	3	2	1		12
SCC						2		2
AGUS-U							1	1
AGUS-H							1	1
Total	48	28	11	4	2	5	2	100

PAP: Papanicolaou, NILM: Negative for intraepithelial lesion or malignancy, AGUS: Atypical glandular cells of undermined significance, CC: Chronic cervicitis, ASCUS: Atypical squamous cells of undetermined significance, LSIL: Low-grade squamous intraepithelial lesion, HSIL: High-grade squamous intraepithelial lesion

Table 4: Correlation of PAP smear and colposcopic finding

PAP smear	Colposcopic finding				
	Normal	ACW	Mosaic	Punctation	Total (%)
NILM	25	22	04	14	65
ASCUS		01	01		02
LSIL	02	10	03	02	17
HSIL		08	04		12
SCC			02		02
AGUS-U		01			01
AGUS-H		01			01
Total	27	43	14	16	100

PAP: Papanicolaou, NILM: Negative for intraepithelial lesion or malignancy, AGUS: Atypical glandular cells of undermined significance, ASCUS: Atypical squamous cells of undetermined significance, SCC: Squamous cell carcinoma, HSIL: High-grade squamous intraepithelial lesion, LSIL: Low-grade squamous intraepithelial lesion

Table 5: Correlation between histopathological finding with colposcopic finding

Histopathological findings	Colposcopic finding				
	Normal	ACW	Mosaic pattern	Punctuation	Total
Chronic cervicitis	25	17	02	09	51
CIN I	04	12	04	06	26
CIN II		07	03	01	11
CIN III		03			03
CIS			02		02
SCC			03		05
Adenocarcinoma		02			02
Total	29	43	14	16	100

CIN: Cervical intraepithelial neoplasia, CIS: Carcinoma *in situ*, SCC: Squamous cell carcinoma

Table 6: Correlation between PAP smear and histopathological diagnosis

Histopathology	Positive	Negative	Total
PAP smear			
Positive	34	02	36
Negative	18	46	64
Total	52	48	100

PAP: Papanicolaou

Table 7: Sensitivity and specificity of PAP smear

Sensitivity	TP/TP+FN	65.38%
Specificity	TN/TN+FP	95.83%
PPV	TP/TP+FP	94.44%
NPV	TN/TN+FN	71.86%
Accuracy	TP+TN/TP+TN+FP+FN	80.00%

PAP: Papanicolaou, PPV: Positive predictive value, NPV: Negative predictive value

In present study white discharge per vaginum (40%) was most common complaint similarly reported by Chaudhary *et al.*,[6] 39%.

In present study, the most common colposcopy finding was acetowhite area (43%), similar study reported by Krishnegowda and Veena[12] 22%.

On PAP smear 64% were reported NILM, and frank malignancy was reported as 2% cases, low-grade squamous intraepithelial lesion and high-grade squamous intraepithelial lesion was reported 17% and 12%, respectively (Graph 2 and Table 8).

A maximum number of cases on histopathological examination were those of infection among them majority had chronic cerivicitis (48%). Cervical Intraepithelial lesions were seen in 43 cases. CIN I were seen in 28 cases and CIN II and CIN III were reported 15%, and SCC and adenocarcinoma were reported 2% cases, respectively. Similar study reported by Bodal and Brar[18] reported adenocarcinoma in 2% cases only (Tables 9 and 10).

Table 8: On comparison with other studies the following results were obtained

Study	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Present study (2015)	65.38	95.83	94.44	80
Chaudhary *et al.*[6]	79.37	81.02	65.79	89.52
Ashmita *et al.*[13]	90.24	72.73	66.6	86.54
Mallur *et al.*[14]	80	81.54	66.67	89.83
Pimple *et al.*[15]	74.5	92.9		
Goyal *et al.*[10]	86	40.5	66.18	66.18
Kushtagi *et al.*[16]	78			

PPV: Positive predictive value, NPV: Negative predictive value

Table 9: Accuracy of PAP smear

Study	Accuracy (%)
Present study (2015)	80
Chaudhary *et al.*[6]	80.5
Ashmita *et al.*[13]	86.54
Mallur *et al.*[14]	80
Boicea *et al.*[17]	98.3

PAP: Papanicolaou

Table 10: Correlation between PAP smear and colposcopy on comparison with other studies

Study	ASCUS (%)	AGUS (%)	LSIL (%)	HSIL (%)	SCC (%)
Present (2015)	3 (3.0)	2 (2.0)	17 (17)	12 (12)	2 (2.0)
Goyal *et al.*[10]	9 (3.0)	1 (0.33)	17 (5.67)	1 (0.33)	
Chaudhary *et al.*[6]	17 (8.5)		10 (5.0)	5 (2.5)	2 (1.0)
Sharma *et al.*[9]	1 (0.04)		214 (9.28)	5 (0.21)	

PAP: Papanicolaou, ASCUS: Atypical squamous cells of undetermined significance, SCC: Squamous cell carcinoma, AGUS: Atypical glandular cells of undermined significance, LSIL: Low-grade squamous intraepithelial lesion, HSIL: High-grade squamous intraepithelial lesion

14% cases were malignant in PAP smear turned out to malignant in histopathology showing strong correlation between PAP smear and histopathology ($P < 0.0001$) by Pearson correlation coefficient factor.

Some of the cases were obscured by blood and inflammation which were missed on PAP smear but proved to be malignant on histopathology.

Table 8 shows sensitivity, specificity, PPV and NPV compared with other studies.

Table 9 shows accuracy of PAP smear compared with other studies.

Table 10 shows correlation between PAP smear and colposcopy on comparison with other studies.

CONCLUSION

The result on current study support, PAP smear demonstrates of premalignant and malignant lesions,

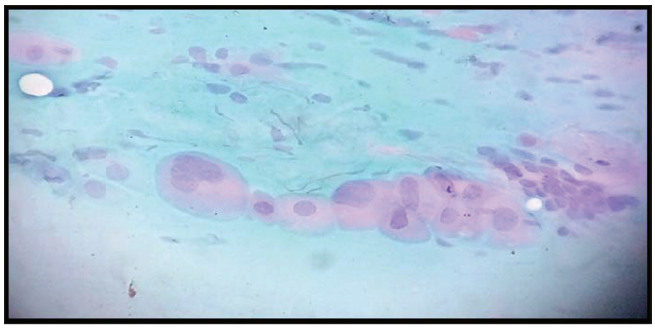


Figure 1: Photomicrograph of papanicolaou (PAP) smear of a case of high grade squamous intraepithelial lesion showing cytoplasm reduced cell borders may be angular or rounded, disproportionate nuclear enlargement, irregular nuclear membrane, abnormal chromatin pattern and tumor giant cell (PAP, ×400)

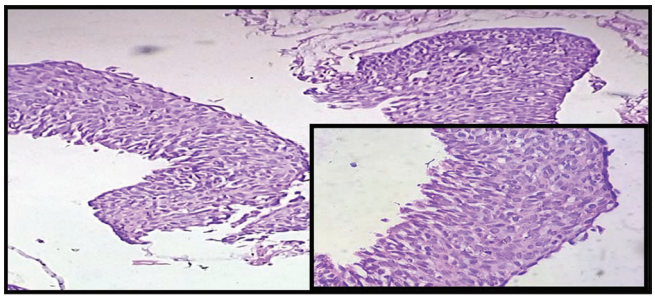


Figure 2: Photomicrograph of histopathology section of a case cervical intraepithelial neoplasia III showing complete replacement of normal squamous cells by crowded abnormal cells with marked nuclear pleomorphism, hyperchromasia, and loss of polarity. No evidence of cell maturation can be seen and the basement membrane is intact (H and E ×100 and ×400)

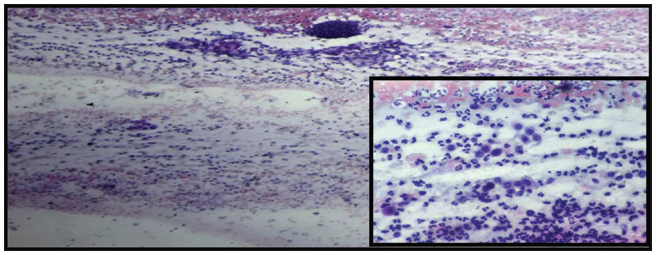


Figure 3: Photomicrograph of papanicolaou (PAP) smear of a case of squamous cell carcinoma showing variation in size and shape dyskaryotic cells with scanty cytoplasm. The chromatin is abnormally clumped (PAP, ×100 and ×400)

whereas colposcopy shows the exact site for biopsy for histopathological diagnosis and for further management. Colposcopy and cytology are not competitive method, but complementary to each other. Best result in early detection of pre-invasive carcinomas could be obtained by combined use of cytology and colposcopic directed biopsy.

The PAP smear screening should be carried out in all women of reproductive and menopausal age group at least once in a lifetime.

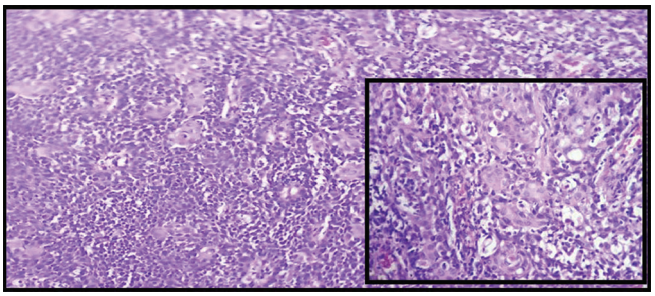


Figure 4: Photomicrograph of histopathology section of a case of squamous cell carcinoma (SCC) showing nests of SCC are invading downward and undermining the mucosa (H and E, ×100 and ×400)

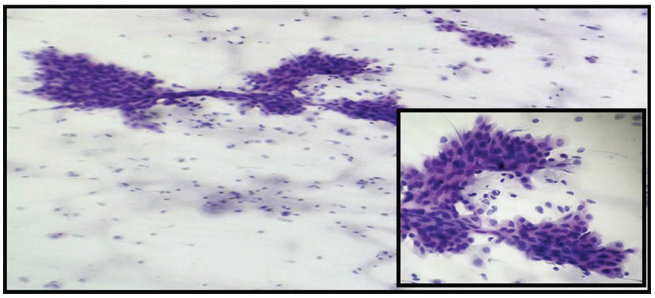


Figure 5: Photomicrograph of papanicolaou (PAP) smear of a case of atypical glandular cells of undermined significance-H showing the individual atypical endocervical cells are hyperchromatic with coarsely clumped chromatin. They show the characteristic feathering of the nuclei at the edge of the cluster (PAP, ×100 and ×400)

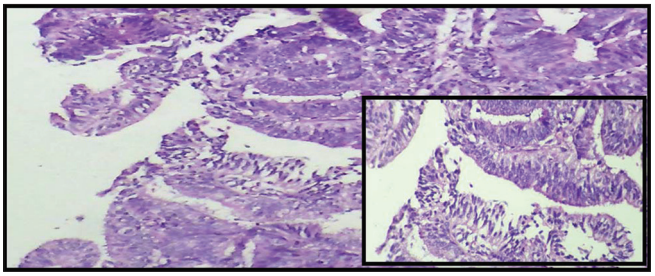


Figure 6: Photomicrograph of histopathology section of a case of adenocarcinoma showing the lining epithelium is stratified and crowded, and it consists of moderately enlarged nuclei with coarse chromatin (H and E, ×100 and ×400)

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Original Article

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Ocular Manifestation in Rheumatoid Arthritis Patients Presenting to Tertiary Care Hospital in South India: A Prospective Study

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Abstract

Introduction: Rheumatoid arthritis (RA) is a systemic inflammatory disease, which is usually associated with a number of extra-articular manifestations, such as pericarditis, pleuritis, major cutaneous vacuities, Felty's syndrome, neuropathy, ocular manifestations, glomerulonephritis, and other types of vacuities.

Aim of the Study: To study the prevalence of ocular manifestations in patients with RA and find out the ocular complications of the routine drug therapy followed to treat RA.

Methods: This is a 1 year prospective clinical study of 50 RA patients, who have attended Ophthalmology Department in Chettinad Hospital and Research Institute. Ocular examination included best corrected visual acuity, color vision, detailed slit lamp and fundus examination, refraction, intraocular pressure measurement, and tests for dry eyes.

Results: About 85% were female patients and 15% male patients. Steroid toxicity in the form of posterior sub capsular cataract was seen in five patients. Chloroquine was used in six patients, out of which one patient developed cornea verticillata and another patient developed bull's eye maculopathy. Ocular manifestations of RA was seen in 32 patients out of which the most common was dry eyes followed by scleritis, episcleritis, iridocyclitis, and secondary glaucoma.

Conclusion: More than half of the patients had ocular manifestations, out of which dry eye was the most common manifestation (90%). The drugs commonly associated with complications are corticosteroids, chloroquine, and hydroxychloroquine. Thus, a regular ophthalmologic evaluation should be done in all RA patients even though they are asymptomatic to ensure early identification of ocular involvement and thus to help alleviate the problems of visual impairment and blindness.

Key words: Chloroquine, Glaucoma, Keratoconjunctivitis, Rheumatoid arthritis, Scleritis

INTRODUCTION

Rheumatoid arthritis (RA) is an autoimmune systemic disease characterized by a symmetrical, destructive, deforming, inflammatory polyarthropathy, in association with a spectrum of extra articular manifestations and circulating antiglobulin antibodies, termed rheumatoid factors (RF).

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The extra articular manifestation includes epericarditis, pleuritis, major cutaneous vacuities, Felty's syndrome, neuropathy, ocular manifestations, glomerulonephritis, and other types of vasculitis.[1,2] The etiopathogenesis of this autoimmune disorder is still unknown. There are many different theories but not proven yet.[3] Extra-articular manifestation in RA are a more common in seropositive patients.[4]

Ocular manifestations seen in RA patients are keratoconjunctivitis sicca (KCS), episcleritis, scleritis, corneal changes, retinal vacuities, and secondary glaucoma. Sjogren first coined the term KCS to describe the tear deficiency as a result of auto immune damage to the lacrimal gland. Dry eye is the most common ophthalmic

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manifestation of RA, with a reported prevalence of 15-25%. Dry eyes due to RA are classified as secondary Sjogren's syndrome.[5]

Episcleritis is sudden in onset and patient complains of discomfort rather than pain. Attacks last 1-2 weeks and are self-limited but recur at intervals of 1-3 months. The prevalence of episcleritis in RA is reported to be about 0.17% and in patients who present to ophthalmology clinic with episcleritis, about 5.6% have RA. Episcleritis could be simple or nodular. About the one-third are bilateral. Treatment of episcleritis is usually unnecessary but in patients with significant discomfort lubricant and topical nonsteroidal agents may be helpful. For recurrent or severe bouts, oral nonsteroidal agents are the preferred therapeutic modality.[6]

Scleritis in RA is associated with a more ominous prognosis than episcleritis. RA is the most common systemic condition associated with scleritis. Patients complain of insidious onset of a deep, boring pain which may radiate to forehead or jaw. Active scleritis involves inflammation of the deep episcleral layer associated with scleral edema. It tends to be bilateral in patients with RA diffuse anterior scleritis is the most common form of scleritis. Nodular scleritis is characterized by firm foci of inflammation which are tender. On involution of the nodules thinning of underlying sclera may occur. Necrotizing scleritis without inflammation also called scleromalacia perforans is characterized by severe thinning of sclera in an otherwise clinically uninflammed painless eye. Necrotizing scleritis is usually associated with wide spread visceral involvement which is associated with high mortality. Hence, the ophthalmologist and rheumatologist should collaborate in the urgent and long-term care of these patients.[7]

Posterior scleritis is often misdiagnosed. It presents as severe orbital pain, proptosis, limited extraocular movement, and uveitis. Decrease in visual activity is dependent on the degree of retinal and choroidal involvement. Ultrasonography is often required for confirmation of the diagnosis.[8]

Involvement of eye in RA can cause severe disability sometimes even blindness.[9] Beside the disease, disease-modifying antirheumatic drugs (DMARDs) particularly chloroquine can also affect vision by deposition over the macula and cornea.

It is important for early diagnosis of RA and send to ophthalmologist for timely intervention and prevent sight threatening complications. The primary physicians need to be aware of these ocular disorders so as to provide appropriate referrals to the ophthalmologist as soon as ocular morbidity is suspected. Conversely, it is critical that ophthalmologists recognize that ocular problems in patients with RA are often indicative of active or ongoing systemic disease.

The objective of the study is to study the prevalence of ocular manifestations in patients with RA and find out the ocular complications of the routine drug therapy followed to treat RA.

METHODS

This is a 1 year prospective clinical study of 50 RA patients who have attended Ophthalmology Department in Chettinad Hospital and Research Institute. Patients of RA attending ophthalmology outpatient department for evaluation of ocular disease and clearance for treatment protocols were included in the study. Patients with juvenile RA (<16 years of age). Dry eyes due to other diseases such as Steven-Johnson syndrome, ocular cicatricial pemphigoid, and chemical injuries, patients with diabetes mellitus, uveitis, scleritis, glaucoma due to causes other than RA were excluded from the study.

History

The demographic details of the patients were recorded. In all cases, a detailed history pertaining to duration of RA, systemic manifestations of RA, drug use and duration of treatment, family history of RA and symptoms pertaining to ocular manifestations were sought.

Ocular Examination

Ocular examination was done to evaluate for the various ocular manifestation like dry eyes KCS, scleritis, episcleritis, peripheral ulcerative keratitis, anterior uveitis and also for ocular complications of systemic treatment. It included best corrected visual acuity, testing for color vision, Amsler's grid, detailed slit lamp examination of anterior segment, detailed fundus examination, refraction, intraocular pressure measurement, and tests for dry eyes. Visual fields and B-scan if necessary were performed.

Tear function tests/dry eye tests included tear break up time (TBUT) and basal Schirmer's test. TBUT was measured as follows: Fluorescein dye was instilled in to the lower fornix, patient was asked to blink several times, tear film was examined with a broad beam and cobalt blue filter, the time interval for the appearance of black spot in the fluorescein stained film indicating the formation of dry areas was noted. TBUT <10 s was considered abnormal (Figure 1).

Basal Schirmer's test was performed using Schimer strips of 35 mm in length and 5 mm in width. After instilling local anesthetic drops (proparacaine), the eyes were gently

dried of excess tears. The Schirmer strip was folded 5 mm from one end and inserted at the junction of the middle and outer third of the lower lid taking care not to touch the cornea. The patient was asked to keep the eyes gently closed. After 5 min, the strip was removed and the amount of wetting from the fold measured. Value of <10 mm at the end of 5 min was considered abnormal (Figure 2).

RESULTS

Among 50 cases included in the study, the number of females were 40 (80%) and males were 10 (20%) In the study, female were predominant as compared to males (Figure 3).

The majority of patients included in the study were in age group of the fifth decade. 20 patients were between 51 and 60 years and <5 patients were seen in <30 years age group. 14 patients were seen in the fourth decade (Figure 4).

Majority of patients in our study had RA for around 1-5 years and only 4 patients had disease for more than 10 years. Hence, only severe sight threatening complications were less in our study (Table 1).

Among total 50 cases of arthritis patients 32 (64%) cases showed ocular involvement. Out of those 32 cases, only 10 had ocular symptoms while 22 were asymptomatic. Patients with episcleritis, scleritis and iridocyclitis were symptomatic.

Among 32 cases with ocular involvement the most common ocular manifestation was dry eye (mild, moderate, and severe forms) followed by episcleritis, scleritis, iridoccyclitis, corneal ulcers, conjunctivitis, and glaucoma (Table 2).

Table 1: Duration of the disease

Duration of disease (years)	Number of patients
<1	7
1-5	21
5-10	18
More than 10	4

Table 2: Ocular manifestation of RA

Manifestation	Number of patients
Dry eyes	27
Scleritis	1
Episcleritis	2
Iridocyclitis	1
Secondary glaucoma	2
Corneal opacity	1
Total	32

RA: Rheumatoid arthritis

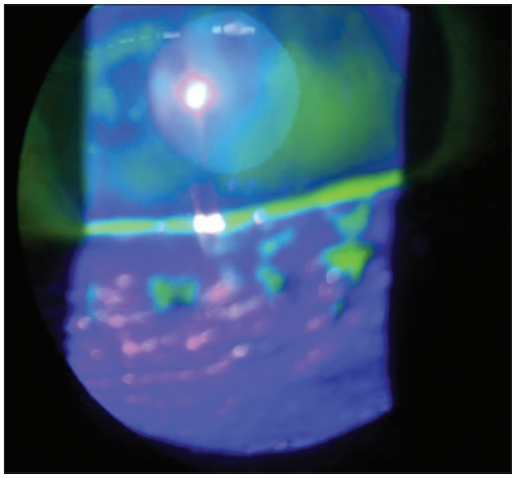

Figure 1: Tear break up time

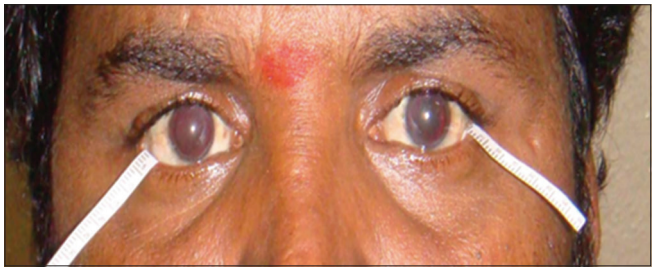

Figure 2: Schirmer's test done in dry eye patient

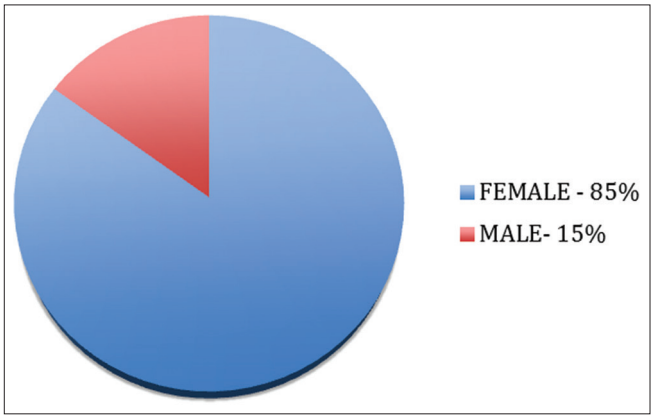

Figure 3: Gender predisposition

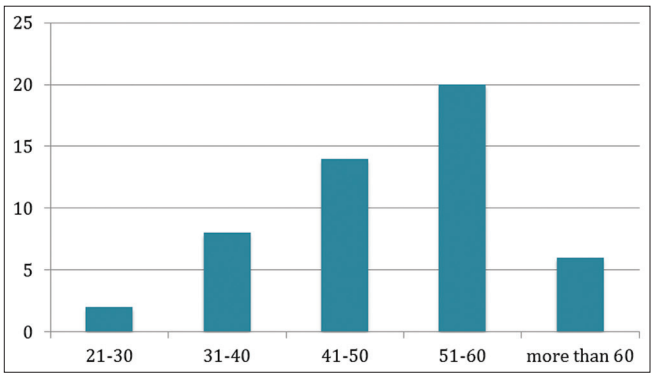

Figure 4: Age group

The complication related to use of drugs for RA also was seen. The patients with RA were commonly using DMARDS, chloroquine, hydroxychloroquine, steroids, nonsteroidal anti-inflammatory drugs, and biological.

Five patients who were on steroids had posterior subcapsular cataract. Steroid induced glaucoma was not seen in our study. Chloroquine was used in six patients, out of which one patient developed cornea verticillata and another patient developed bulls eye maculopathy (Figures 5 and 6). Both the patients were using chloroquine for a more than 8 years without any follow-up or ophthalmological evaluation.

DISCUSSION

RA is usually a more common in women with a ratio of 3:1 and disease onset is in the fourth and fifth decades. In our study, also females were affected more than males.

Reddy *et al.*, study shows that 13 out of 100 patients of RA 39% were found to have eye involvement.[10] The prevalence of different ocular manifestations in this arthritis has been reported differently in different studies. The result of the present study showed 32 (64%) cases out of 50 with ocular involvement. Many of the patients with ocular findings did not have ocular complaint and was detected by routine checkup. Out of 32 cases with ocular involvement 32% cases had symptom while the previous study showed only 37.28% complained of ocular symptom.

Figure 5: Nodular episleritis in one patient

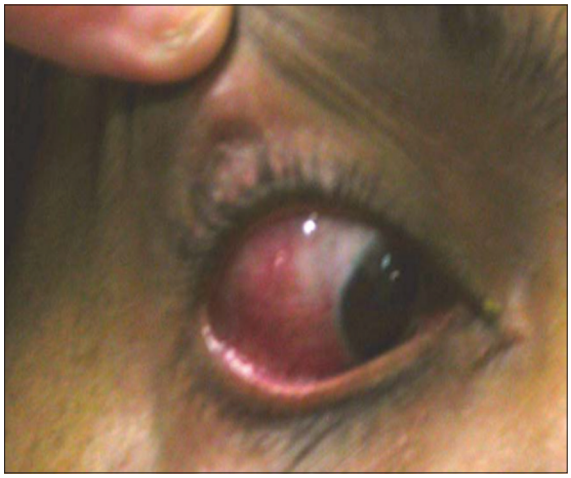

Figure 6: Anterior scleritis in one patient

Moss *et al.*, studied 3,722 individuals and found that 14.4% of patients had dry eyes.[11] Females had more incidence of dry eye (16.7%) compared to males (11.4%). They concluded that the risk factor for developing dry eye was arthritis which was followed by gout. In our study, the most common ocular manifestation was dry eye 44% (22 cases), followed by episcleritis, scleritis and corneal ulcer, viral keratitis, and conjunctivitis.

RA is seen a more common in fourth and fifth decades. Our study showed that majority of the patients with RA was in their fifth decades which comprised 40% (20 cases) with female predominance 4:1. Among 32 cases of RA with ocular involvement, the highest incidence of ocular manifestation was also seen in the fifth decade.

KCS or dry eye is the most common ocular manifestation of RA with reported prevalence of 15-25%.

Watson and Hayreh did a 10 years study of 207 episcleritis and 159 scleritis patients.[12,13] RA was seen in 28 patients in there study group. Seven had out episcleritis, eight with diffuse anterior scleritis, four with nodular anterior scleritis, three with necrotizing scleritis, and six with scleromalacia perforans.

Jabs *et al.*, studied 134 patients with scleral inflammation over a 12-year period.[14] 134 patients were studied and 37 patients had episcleritis and 97 had scleritis. Systemic rheumatic disease was seen in 30% with episleritis and 39.2% with scleritis. The rheumatic disease most common associated with scleral inflammation was RA.

In our study, 32 patients had ocular involvement and in that 4 had episcleritis and 2 had scleritis. Necrotizing scleritis with inflammation and scleromalacia perforans were not seen in our study as these complicated conditions were found in patients with long duration of arthritis with severe forms and in long term untreated cases.

McGavin *et al.*, did a study on 4210 patients with RA and results showed that 7 patients had episcleritis 28 patients had scleritis.[15] Similarly, they found co-existent posterior scleritis was more common in rheumatoid scleritis (22.2%) than in nonrheumatoid scleritis (5.6%). Our study revealed that among 32 RA

patients with ocular manifestation only five (20%) had anterior uveitis but band shaped keratopathy was not noted along with it.

Cases of glaucoma secondary to scleritis and episcleritis have been reported in different studies. In our study secondary glaucoma due to uveitis was noticed in two patients with RA.[16] RF was negative in 22 (44%) of patients with juvenile RA.

Most of the patients of RA patient referred to us were mainly to rule out chloroquine toxicity.

Steroid toxicity in the form of posterior sub capsular cataract was seen in five patients. Chloroquine was used in six patients, out of which one patient developed cornea verticillata and another patient developed bulls eye maculopathy (Figure 7 and 8). Both the patients were using chloroquine for more than 8 years without any follow-up or ophthalmological evaluation. If the cumulative dosage of chloroquine exceeds more than 300 g over period of 5-year, then chances of ocular complications are more.[17] Same thing holds good for hydroxychloroquine use for more than 7 years, dose more than 6.5 mg/kg/dose with cumulative dose more than 1000 g can lead to complications.[18]

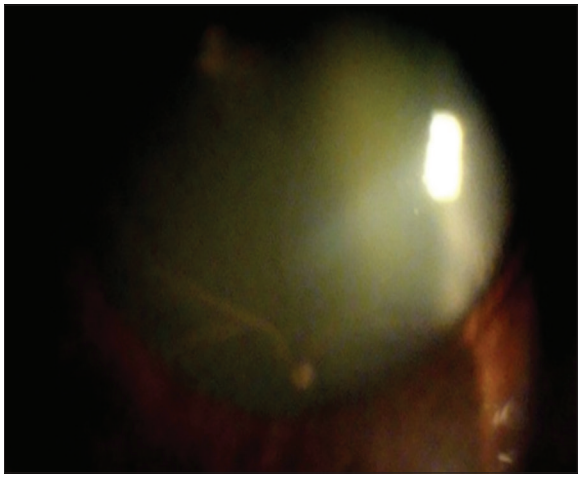

Figure 7: Cornea verticillata in one patient

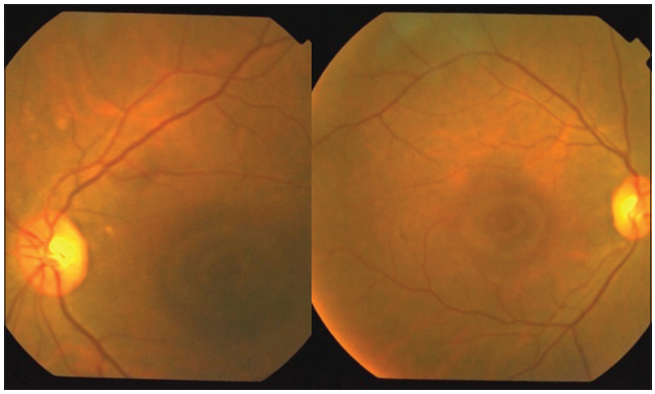

Figure 8: Bulls eye maculopathy

CONCLUSION

Ocular manifestations are common. More than half of the patients (52%) had ocular manifestations, out of which dry eye was the most common manifestation (90%).

Dry eyes are directly related to duration of disease than the severity. Routine Schirmer's test and Rose Bengal staining help to detect the early onset of dry eye syndrome in patients with RA and start treatment. Ocular complications associated with the systemic treatment of RA are well-known. The drugs commonly associated with these complications are corticosteroids, chloroquine, and hydroxychloroquine.

Thus, regular ophthalmologic evaluation should be done in all patients even though they are asymptomatic to ensure early identification of ocular involvement and thus to help alleviate the problems of visual impairment and blindness.

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Original Article

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Births Should Not Cause Deaths: A Retrospective Analysis of Maternal Mortality at a Tertiary Care Hospital in Eastern India

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Abstract

Introduction: Pregnancy, although being considered a physiological state, carries the risk of serious maternal morbidity and at times death. This is due to various complications that may occur during pregnancy, labor or thereafter. Maternal death has serious implications for the family, the society, and the nation. Maternal mortality is universally considered as human development indicator in a country and determines the health status of the people.

Method: A retrospective hospital-based study of 65 maternal deaths was conducted over a period of 1-year from January 2014 to December 2014 in respect to maternal age, parity, booking status, residence, referral, socioeconomic class, admission death interval, and cause of death.

Result: Over the study period, there were 6277 deliveries, 5761 live births, giving a maternal mortality ratio of 1035 per 100,000 live births. Eclampsia was the leading direct cause and anemia the leading indirect cause. The age group of 20 to 30 years was crucial. The majority were primi, and most deaths were in unbooked cases transferred from outside.

Conclusion: Most maternal deaths are preventable by optimum utilization of existing maternal and child health care facilities, identifying the bottlenecks in health delivery system, early identification of high-risk pregnancies, and their timely referral to the tertiary care center.

Key words: Anemia, Eclampsia maternal death, Mortality rate, Sepsis

INTRODUCTION

Maternal mortality as defined by WHO is "the death of any woman while being pregnant or within 42 completed days of termination of pregnancy, irrespective of the duration and the site of pregnancy, from any cause related to or aggravated by the pregnancy or its management but not from accidental or incidental causes."[1] Maternal mortality is defined internationally, as maternal deaths per 1, 00, 000 live births.

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Direct maternal death is the result of a complication of pregnancy, delivery, or their management. Indirect maternal death is a pregnancy-related death in a patient with pre-existing or newly developed health problem.

An estimated 2, 87, 000 maternal deaths occurred worldwide in 2010, most of which were in low-income and middle-income countries and were avoidable.[2] More than 800 women die per day, more than 30 die every hour. More than 85% die in sub-Saharan and south Asian regions. According to data published by Sample Registration System, India in December 2013,[3] the maternal mortality rate in India is 178, with the highest maternal mortality ratio (MMR) in Assam (328) and lowest in Kerala (66). The states of Jharkhand/Bihar stand at MMR of 219 which is higher than the national average.

UN millennium development goals (MDG) has made the reduction of maternal mortality rate as a global health

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priority.[4] To reach the target of the fifth MDG a 75% decrease in MMR between 1990 and 2015 is needed.

The high number of maternal deaths in some areas reflects inequities in access to health services and highlights the gap between the rich and poor. Maternal death has serious implications for the family, the society, and the nation. This present study was conducted to review the existing MMR and the causes of maternal death at a tertiary care hospital of rural India. So that corrective measures can be taken to reach the goal within the stipulated time frame as most of the deaths are preventable.

MATERIALS AND METHODS

This retrospective hospital-based study was carried out in the Obstetrics and Gynecology Department of Rajendra Institute of Medical Sciences, a tertiary care hospital in Jharkhand, India over a period of 1-year from 1st January 2014 to 31st December 2014. A total of 65 maternal deaths were analyzed with special emphasis on socio-demographic profile of the patient, prenatal care, parity, cause of death, time interval from admission to death, and communication facility and delay if any in reaching the tertiary care teaching hospital from the primary care center.

RESULTS

There were 65 cases of maternal mortality among 5761 live births and 6277 deliveries over the period of study giving an MMR of 1035 per 1,00,000 live births. Of these, 30 deaths (46.1%) were due to direct causes and 35 deaths (53.9%) were due to indirect causes.

The majority of deaths 31 were in the age group of 20-25 years.

The majority (51%) of the mothers who died belonged to the lower socioeconomic strata of the society.

Maximum patients (65%) were primigravida.

Maximum of the patients died within 6 h of admission.

The major cause of maternal mortality was eclampsia and pre-eclampsia.

The most prominent indirect cause for death was anemia.

75% of patients had hemoglobin <8 g%.

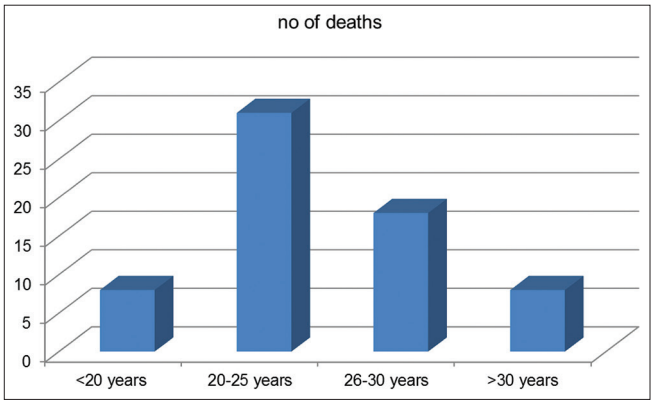
DISCUSSION

The maternal mortality rate at teaching hospitals in India is very high. Death of mother is a tragic event. A vast majority of maternal deaths are preventable. High maternal mortality indicates poor maternal and child health care (MCH). This tragedy has immense effects on the family, especially on the child.

In the present study, there were 65 maternal deaths among 6277 deliveries, giving an MMR of 1035 per 1, 00, 000 live births, which is higher than national averages. Rajendra Institute of Medical Sciences being a teaching institute and a tertiary care center gets complicated cases from rural areas. Admissions of moribund cases referred from the peripheral hospital have inflated this mortality ratio, like other teaching institutions of India. Like our study, other similar studies[5-7] from tertiary care institution reported MMR being higher than the national average. This variation could be explained due to many variables, might be due to the effect of Janani Suraksha Yojana (JSY), under National Rural Health Mission, which on one side has tried to promote institutional deliveries to avert maternal deaths, on the other hand maximally unbooked complicated patients reaches hospital in moribund state, without any antenatal visit.[8] Promotion of transport vehicles also improved death reporting by carrying complicated cases such as postpartum hemorrhage, eclampsia which previously use to die in the anonymity of their home or on the way to seek help at a medical facility.

Our study showed that 75.38% of women died between the ages of 20-30 years (Graph 1), as the highest number of women belong to this age group. Our 75.38% figure is closer with Puri *et al.*,[9] at 71.53% and Ashok *et al.*,[7] at 78.5%.

Multigravidas (Chart 1) comprised 35% while primigravidas 65% of the total deaths in our setup. On the contrary studies done by Purandare *et al.*,[10] and Pal *et al.*,[11] majorities



Graph 1: Distribution of maternal deaths according to age group

of the deaths were reported in multipara (70% and 76%). Ashok *et al.*,[7] observed that 50.8% of women who died were multipara.

The majority of deaths (93.85%) were in women belonging to low socioeconomic status (Chart 2). A similar observation was made by Ashok *et al.*,[7] (61.5%) and Purandare *et al.*,[10] (70%).

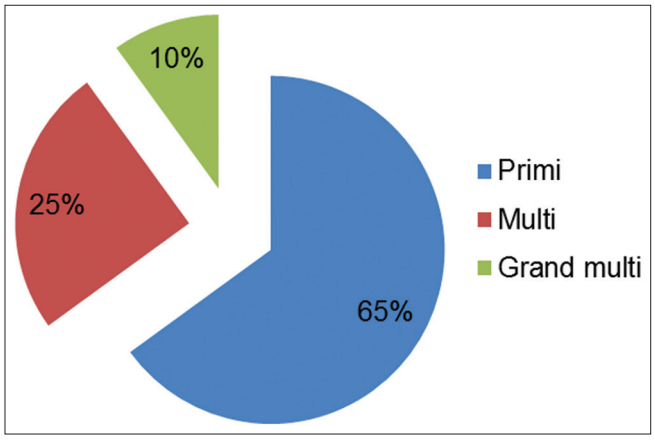


Chart 1: Distribution of maternal deaths according to parity

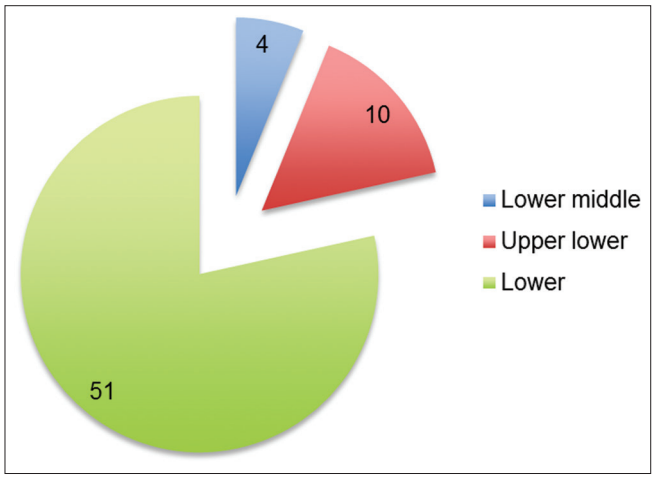


Chart 2: Distribution of maternal deaths according to socioeconomic status

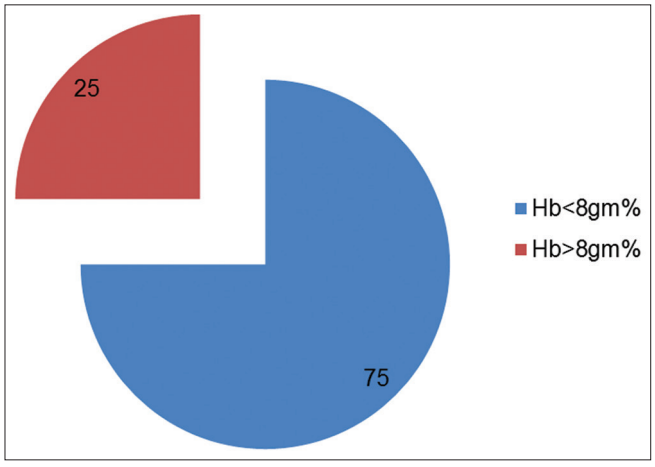


Chart 3: Distribution according to anemia status

Very high percentage of unbooked patients in maternal deaths (80%) highlights the importance of adequate antenatal care. A similar observation of majority of mothers who died being unbooked was also made by various other studies.[7,9-11] Guin Gita *et al.*,[8] in their study of the role of JSY on maternal mortality have also stated the importance of antenatal care in reducing MMR. They state that unfortunately JSY has put an undue stress on institutional delivery without making a sincere effort to promote the importance of antenatal care for reducing maternal mortality and morbidity.

The majority of women (Table 1) died within 6 h of their reporting to the hospital as most were brought in a highly moribund state where nothing much could be done to save them. Similar data was presented by Ashok *et al.*,[7] and Purandare *et al.*,[10] (57% within 6 h). In our study, 62% of the patients died within 6 h of admission further highlighting the need for adequate and quick transport facilities and timely referral from peripheral centers for high-risk patients.

Table 1: Distribution according to time interval from admission to death

Time interval from admission to death	Number of maternal deaths	Percentage
0-30 min	5	7.69
30 min-6 h	35	53.84
6-24 h	20	30.76
>24 h	5	7.69

Table 2: Distribution of maternal deaths according to direct causes

Cause of death	Number of death	Percentage
Eclampsia and pre-eclampsia	13	20
Sepsis	9	13.8
Hemorrhage	4	6.2
Amniotic fluid embolism	3	4.6
Unsafe abortion	1	1.5

Table 3: Distribution of maternal deaths according to indirect causes

Causes of death	Number of deaths	Percentage
Anemia	26	40
Heart disease	4	6
Renal disease	2	3
Complicated malaria	1	1.53
Cerebrovascular accident	1	1.53
Sickle cell crisis	1	1.53

In the present study (Table 2), direct causes contributed to 46.1% of maternal deaths, of which eclampsia (20%) is the most common. This is in contrast to most of the studies[7,10,11] where hemorrhage was the major direct cause of maternal mortality. Guin Gita *et al.*,[8] and Bedi *et al.*,[5] had also reported pre-eclampsia/eclampsia as a major direct cause of maternal mortality in their study. Puri *et al.*,[9] have stated sepsis being the major cause of maternal death in their study with pregnancy induced hypertension as second and hemorrhage being the third. Hemorrhage was the major cause of maternal death in most studies and the third most common cause in our setup at 6.2% of the total deaths. This could be because of proper management of the third stage of labor and an efficient and well-equipped blood bank to save mothers from major blood losses and subsequent deaths. Five patients died before blood could be made available, so it becomes apparent that many of the deaths that occurred could have been avoided if they were transferred earlier (Table 3).

Indirect causes (Table 3) accounted for 53.9% of maternal deaths, anemia being the underlying cause in 40% cases. The major indirect cause of death in most studies[7,8,10,11] was anemia with the percentage varying from 15% to 65%. Correction of anemia at grass root level is very important to prevent these deaths. MCH is essential as regular ANC check-ups can help detect and correct anemia.

Another major and easily preventable cause of maternal death is sepsis. Most of these women had delivered at home and had poor antibiotic availability.

In summary, improvements in maternal nutrition; early identification and registration of all pregnant women in the first trimester of pregnancy; identification of high-risk pregnancies promptly and referred in time to a hospital for appropriate interventions and management, including swift access to lifesaving technology are available if things go wrong; would be the measures needed to make motherhood safe. Obstetricians and public health planners will need to identify women at an elevated risk of maternal death and to develop prevention strategies to avoid the conditions that cause these deaths.

CONCLUSION

The MMR in our study is higher than the national averages. Most deaths could have been avoided with the help of good antenatal, intranatal and postnatal care, early referral, quick, efficient and well-equipped transport facilities, availability of adequate blood and blood components, and by promoting overall safe motherhood. To reduce maternal mortality and morbidity, the main thrust should be on implementing basic and comprehensive obstetrics care. Analysis of every maternal death through maternal death audit, either at the community level or at the institutional level should be carried out. It will help in identifying the actual cause of maternal deaths and deficiencies in the health care delivery system that might contribute in formulating preventive measures to reduce pregnancy-related deaths.

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Original Article

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Prevalence of Neck and Lower Back Pain among Dentists from Three Dental Colleges in Patna City: A Questionnaire Study

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Abstract

Introduction: In the practice of dentistry, stress, tension, and postural practices can contribute to neck and lower backache problems. Considering the importance of this problem, we considered it was necessary to investigate the prevalence and severity of these problems in this part of eastern India.

Purpose: To assess the prevalence, severity, and extent of lower back and neck pain among dentists of three dental colleges of Patna and to suggest/advice preventive measures.

Materials and Methods: 121 dentists from three dental colleges in Patna were surveyed to determine the prevalence of neck and lower back pain (73 males and 48 females). The dentists were interviewed with the help of a questionnaire.

Result: The data obtained and showed that (88) 72.80% of the dentists had suffered with the problem, sometimes during their practice of dentistry. 38.01% of dentists complained of the lumbar pain. 13.02% had pain in the cervical area, and 24.04% of the dentists had pain in both the areas. Only 39.54% of those complaining of a backache sought medical help. 57.85% of dentists opted exercise and yoga as treatment modalities to relieve the pain.

Conclusion: The neck and lower back pain is largely prevalent in dental practitioners though not of very severe degree. Preventive aerobic and relaxation exercises should be included in weekly activities of dentists to prevent recurrence of this problem.

Key words: Dentists, Exercise, Low back pain, Musculoskeletal disorder, Neck pain

INTRODUCTION

The dentists are at high risk of neck and lower backache problems due to the limited work area with a limited scope of movement and narrow visual field associated with the oral cavity. These working restrictions frequently cause a clinician to assume stressful body positions to achieve good access and visibility inside the oral cavity. Furthermore, dental procedures are usually long; require much more concentration during work.[1] Dentist often cannot avoid prolonged static postures. Even in optimal seated postures, more than one-half of the body's muscles are contracted statically, and there is little movement of the vertebral joints. This may result in damaging physiological changes (micro changes) that can lead to back, neck or shoulder pain or musculoskeletal disorders (MSDs) (macro changes)[2] in dentistry, overstrained and awkward postures, repetitiveness of different joint movements, use of high frequency vibration tools, and psychological stress have been identified as risk factors.[3,4] Studies have shown that dentists report more frequent musculoskeletal pain[5,6] particularly back and neck pain, has been found to be a major health problem for dental practitioners.[7,8] its exact causes are legion, and an exact diagnosis is often difficult.

It has been stated that the most common sites of pain among dentists are in the areas of the cervical and lumbar vertebrae.[9-11] It has been pointed out that common postural

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faults among dentists are craning and/or excessive bending and twisting of neck, bending forward from the waist, elevation of shoulders, and general bending or twisting of the back and neck.[12]

As preventive measure dentists should be taught relaxation techniques early in clinical training, and they should be taught correct working posture at chair side.

Recently, "Ergonomics" has become a popular term. The term has been used in most professions, but increasingly in the dental profession. It is a discipline that studies workers and their relationship to their occupational environment. This includes many different concepts such as how dentists position themselves and their patients, how they utilize equipment, how work areas are designed, and how all of these impact the health of dentists.[2]

It is very important to maintain an adequate work posture and that the instruments and furniture that the dentist is working with have adequate working characteristics.[13] Furthermore, they are exposed to biomechanical risk factors, which indicate that work forced postures, would imply more risk of soreness and presence of skeletal muscle lesions. These lesions could begin to appear at the beginning of their clinical practice as students, by acquiring inadequate postures and working habits that will accompany them for the rest of their professional life, acquiring an unhealthy lifestyle in their work environment.[14]

However, there is a lack of data regarding musculoskeletal pain among the Dentists in Bihar. Hence, the need was felt to conduct a study to check prevalence and risk factors associated with MSD among dentists.

This questionnaire study was taken to assess the prevalence, severity, and extent of lower back and neck pain among dentists from three dental colleges in Patna and propose some preventive measures.

MATERIALS AND METHODS

A "pilot" study was conducted on 21 dentists from three dental colleges in Patna. The survey was conducted on the 15th and 16th July 2015; using printed questionnaire. Based on the data obtained from 'pilot' survey, modifications were made to make the main survey more reliable.

The main survey was a questionnaire study. The survey was conducted from 7th August 2015 to 28th August 2015 on a sample of 132 dentists out of which 52 were females and 80 were males.

The questionnaire used for the study consisted of 6 questions about general information and 14 questions about specific information on neck and lower back pain. The dentists were also enquired about any treatment modality opted.

The questionnaire was printed in the English language. All questions were the close ended type.

The dentists were selected from the following three dental colleges of Patna city:

1. Buddha Institute of Dental Sciences and Hospital
2. B. R. Ambedkar Dental College
3. Patna Dental College and Hospital.

The study protocol was reviewed and approved by Ethical Committee of the Institute.

The selection of these colleges and Dentists was dependent on the consent to participate in the study. During the survey, the majority of dentists were enthusiastic and had a positive attitude.

The questionnaire used to collect data for this study was based on similar studies published previously (2, 3, 5, 6). The study fully complied with the ethical standards for human research. The questionnaire included 20 questions pertaining to three domains, demographic and professional characteristics, general medical history, and history of MSD before and after joining the dental profession. These domains included questions pertaining to work setting characteristics and the effect of MSD on dentists' daily work and non-work activities. MSD was defined as any unpleasant sensation in the musculoskeletal system of the body developed after joining the dentistry profession.

The questionnaire was sent self along with a reply paid envelope and an explanation of the purpose of the study to 132 dentists working in Dental colleges of Patna, inviting them to participate in the study. Respondents were assured of the confidentiality of their information. Dental professionals involved in direct patient contact for at least 10 h per week were eligible to participate. The participants had to complete the questionnaire. Incomplete questionnaires were rejected. 126 dentists replied and participated in the study. After checking, we excluded five questionnaires due to incomplete response. 121 questionnaires were complete and were used for analysis.

RESULTS

- Figure 1 shows 73% of dentists complained of lower back and neck pain while 27% did not have lower back and neck pain

- Figure 2 shows 60% of males and 40% of females suffered with neck and lowered back
- Graph 1 shows 38% complained lumbar pain, 13% of cervical pain, 22% of both, and 27% were recorded as none
- Graph 2 shows 40% complained of mild pain in lower back and neck region, 31% of moderate nature, 2% of severe nature, 27% did not complained of any pain
- Table 1 shows 76.03% of dentists in 21-30 years age group reported of pain in lower back and neck region 20.67% in 31-40 years age group. Above 40 years were 3.30%
- Table 2 shows in 38.84% of dentists professional life was affected
- Table 3 shows 35.54% had consulted physician
- Table 3 shows 74.38% dentists had taken precautionary measures while 25.62% did not take any precautionary measure
- 57.85% of dentists opted exercise and yoga as treatment modalities to relieve the pain.

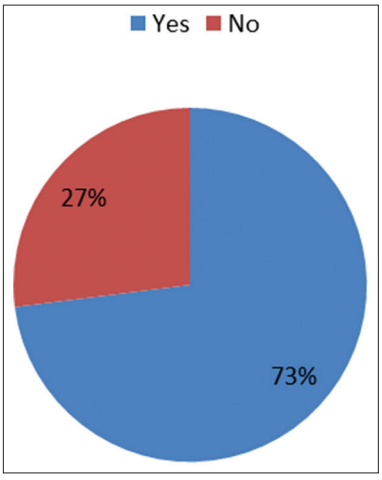


Figure 1: 73% of dentists complained of lower back and neck pain while 27% did not have lower back and neck pain

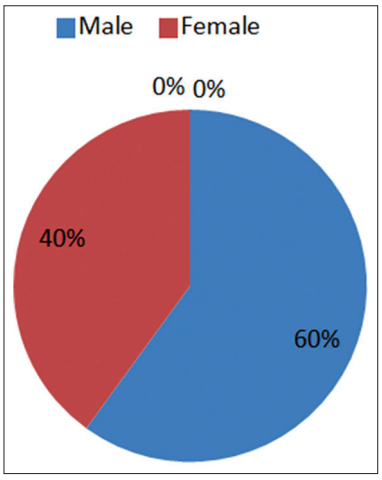


Figure 2: 60% of males and 40% of females suffered with neck and lower back

Table 1: Prevalence of neck and lower back pain among various age groups of dentists

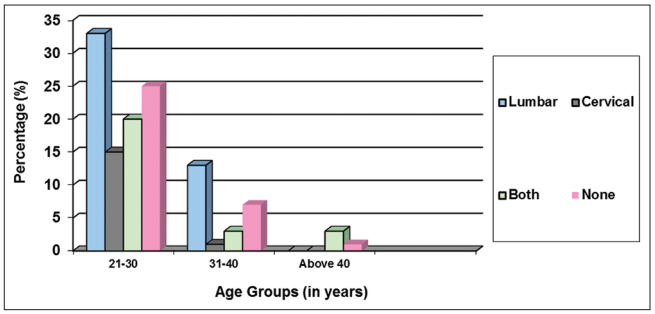
Age groups (years)	Number	Percentage
21-30	92	76.03
31-40	25	20.67
40	4	3.30
Total	121	110

Table 2: Neck and lower back pain affecting professional life of dentist

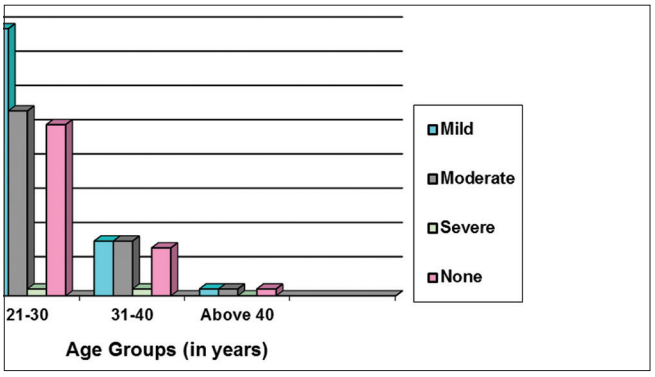
Areas	Professional		Life	
	Yes	No	Yes	No
Cervical	09	08	06	10
Lumbar	21	24	14	32
Both	17	09	14	12
None	-	33	-	33
Percentage	38.84	61.16	28.09	71.91

Table 3: Dentist who have consulted or taken precautionary measure for lower back pain

Areas	Precautionary		Consulted	
	Yes	No	Yes	No
Cervical	11	5	8	8
Lumbar	38	8	22	24
Both	20	6	13	13
None	21	12	-	33
Total (%)	90 (74.38)	31 (25.62)	43 (35.54)	78 (64.46)



Graph 1: Neck and lower back pain in relation to age groups



Graph 2: Relation between severity of lower back and neck pain with age groups

Graph 1 shows: (1) 38.01% of dentists complained of lumbar pain and 13.02% complained of cervical pain, 21.84% complained of both (lumbar and cervical), and 27.20% did not complain, (2) 33 dentists had lumbar pain, 15 had cervical pain, 20 had both, and 25 did not have any pain in age group 21-30 years, (3) 13 dentists had lumbar pain, one had cervical pain, 3 had both, and 7 did not have any pain in age group 31-40 years, (4) 3 had both (cervical and lumbar pain) and 1 did not have any pain in age group above 40 years.

Graph 2 shows: (1) 39.88% dentists had mild lower back and neck pain, 30.98% had moderate pain, 1.88% had severe pain, and 27.20% did not complain of any pain, (2) 39 dentists had mild lower back and neck pain, 27 had moderate pain, 1 had severe, and 25 did not had any pain in age group 21-30 years, (3) 8 dentists had mild lower back and neck pain, 8 had moderate pain, 1 had severe pain, and 7 did not complained of any pain in age group 21-30 years, (4) 1 dentist had mild lower back and neck pain, 2 had moderate pain, and 1 did not complained of any pain in age group 21-30 years.

DISCUSSION

MSD have become increasingly common worldwide during the past decades. It is a common cause of work-related disability among workers with substantial financial consequences due to workers' compensation and medical expenses.[15] In dentists, overstrained and awkward back postures for back pain, repetitiveness for neck and shoulder disorders, and psychosocial stressors for back, neck and shoulder complaints.[14] A slight hand neuropathy has also been reported caused by exposure to high frequency vibration tools.[16]

A cross-sectional study was carried out to assess the prevalence of pain and risk factor associated with the MSDs among the dental surgeons of three dental colleges in Patna.

The majority of the patients (73%) surveyed were found to be suffering from MSDS. Shaikh *et al.* also reported a high incidence (80%) of MSDS in their study in 30 dentists.[16] Among the MSDS, the incidence of low back pain (73.3%) was highest. Various other studies also suggest high incidence of MSDS among dentists.[17,18]

60% of males and 40% of females suffered with neck and lower back. These results are similar to the results of study done by Al Wazzan *et al.*, with findings - 58.24% males and 41.75% females suffered with neck and lowered back pain.[1]

The most common site for MSDS was lower back (38%), i.e., lumbar pain. 13% experienced cervical pain while 22% experienced pain in both regions. These results are again consistent with other studies where the most common area involved was lumbar region.[19] On the contrary, Leggat and Smith reported high incidence of cervical pain as compared to lumbar pain.[17]

The severity of pain encountered by dentists in our study varied from mild to severe. The majority of the dentist (40%) experienced mild pain which subsided with rest and 2% experienced severe pain. The severity of MSDS as found in our study was low as only 35.54% sought medical intervention, and only 38.84% reported that their professional life was affected. Khalid *et al.*, in their study, reported that only 37% of those suffering back and neck pain sought medical treatment and concluded that these symptoms among dental personnel are not severe enough to ask for medications.[1]

Most of the respondent in our study were a young practitioner (21-30 years). However, no correlation was found between age and severity or incidence of pain.

The majority of the dentist opted exercise and yoga as treatment modalities to relieve the pain and reported having used precautionary measures like periodic breaks, working in indirect vision.

Recommendations

Within the limitations of this study, it might be concluded that neck and back pain among dental personnel of 3 dental colleges are not of a severe nature in Patna.

However, to minimize or even prevent such ailments, preventive aerobic and relaxation exercises should be included in the weekly activities of dental personnel. Such a practice would (1) help dental professionals avoid future physical limitations or handicaps, (2) help them remain productive for longer periods of time during their professional lives, and (3) also help to improve the quality of care during clinical procedures.

Aerobic Exercises

Aerobic exercise has been reported to improve or prevent back pain. In general, exercise programs that facilitate weight loss, trunk strengthening, and the stretching of musculotendinous structures appear to be helpful in alleviating low back pain. A 30 min aerobic program three times a week is ideal for overall fitness.

Exercise to promote the strengthening of the muscles that support the spine (i.e., the oblique abdominal and spinal extensor muscles) should be considered (Figures 3 and 4).

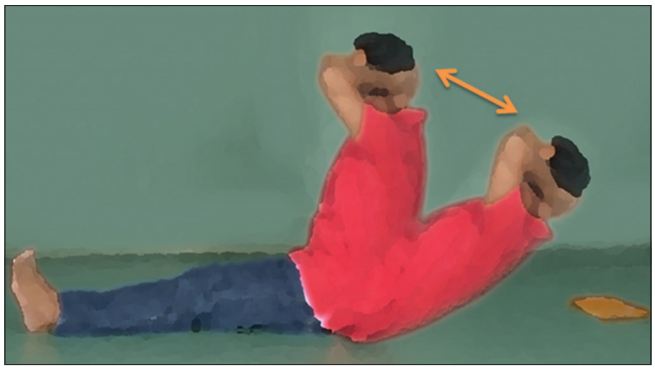


Figure 3: Trunk muscles exercise. Lie in supine position with both hands behind back of your neck. Then up right yourself to a sitting position. Legs should be on the floor during the up righting movement. You can asked somebody to stabilize your legs. If you cannot reach the sitting position, you can do it half way, i.e., to 45°

Figure 4: Trunk muscle exercise: Lie in supine position AND, raise your legs up to 45° from the floor, without bending your knees, make a circular movement of 30 cm. In diameter 5 times clockwise and 5 times counter clockwise. Take rest for few seconds, and then repeat the exercise

An effective program may include a warm-up period, about 30 min of aerobic activity, isolated muscle group work (trunk muscle), and a cool-down period walking and/or water exercise are also recommended.

Dental professional may need to take a break from exercise if it aggravates back pain. It is recommended that dental professionals confirm with their doctor regarding which exercise should be used to relieve back pain, to stay fit, and prevent pain injuring oneself again. The presence of any leg pain or other evidence of nerve injury should serve as an indication to consult a physician before beginning exercise.

Relaxation Exercises

Stress may produce a state of chronic muscle contraction that may decrease circulation increase the concentration of the toxic products (lactic acid and potassium ions) of muscle activity. These toxic products may in turn stimulate nerve endings to generate low back pain. Deep breathing and progressive muscle relaxation exercises may serve to diminish this stress reaction. Below are some brief relaxation exercise that dentists and their auxiliary personnel may wish to employ any time during the day, break time, or in among patients.

Exercise 1: Performing a breathing exercise is one of the simplest ways to relax in any situation. Take 5-10 min to sit quietly and breathe deeply. Here is an example. Close your eyes and take a long, deep breath. Let it out very slowly. Now, take a second long, deep breath, as you let it out, feel yourself releasing the tensions in your mind and in your body. Just let yourself relax more and more, as you continue.

Exercise 2: Clench your hands. While keeping them clenched, pull your forearms tightly up against your upper arms and raise your shoulders against your neck. While keeping those muscles tense, tense all the neck, back, and leg muscles. While keeping all these tensed, shut your eyes fairly tight and take deep breath and hold it for 5 s. Then, let everything go all at once. Feel yourself letting your tensions.

CONCLUSION

The present study was conducted on 121 dentists from three dental colleges in Patna to assess severity and area of the neck and lower back pain.

For dentists, neck and lower back pain is not a new problem, nearly most of the dentists have suffered from it sometimes during their practice of dentistry. Lower back pain is more prevalent than neck pain mainly due to faulty postural habits.

It can be concluded that neck and back pain among dentists is not of severe nature. The neck and lower back pain is largely prevalent in dental practitioners. That brings along with it a considerable amount of discomfort, lost working time, and economic loss. What we need is not preventing its incidence and recurrence by including preventive aerobic and relaxation exercises in weekly activities of dentists. This will help in improving the quality of work in their clinical practice.

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Original Article

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Intraoral Cystic Lesions: Presentation of a Series of 54 Cases and Review of Literature

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Abstract

Introduction: Congenital cystic swellings can be classified into dermoid cysts, congenital ductal cysts, and branchial cleft anomalies like cystic hygroma. These cysts are composed of elements from all three germinal layers. Acquired cysts most common encountered are mucous retention cysts usually involving the minor salivary glands.

Objectives: A retrospective review of 54 cases of intraoral cystic swellings of the floor of the mouth is presented, evaluating their successful diagnosis and further the different surgical approaches for their removal.

Materials and Methods: A total of 54 cases presented with a diagnosis of cyst of the floor of the mouth, treated at Saraswathi Institute of Medical Sciences, Hapur, Uttar Pradesh, India, between the period of 2010 and 2014.

Results: Out of the total 54 cases diagnosed with intraoral cystic lesions, 30 cases were male and 24 cases were female which showed male:female ratio of 1.25:1. Age distribution of the patients ranged from 18 months to 62 years.It was seen that 16 patients belonged to the age group of 18 months-15 years (29.6%), 20 between 16 and 30 years (37.1%), 12 between 31 and 45 years (22.2%), and 6 patients were between 46 and 62 years of age (11.1%). Out of the 54 cases, 16 were ranula, 10 cases were of simple ranula (18.5%) and 6 were of deep plunging ranula (11.1%), 6 cases were of dentigerous cyst (11.1%), 10 cases of dermoid cyst (18.5 %), 2 parasitic cysts (3.7%), 14 cases were of mucus retention cyst (25.9%), and 6 were of cystic hygroma (11.1%).

Conclusion: Surgery is the treatment of choice for intraoral cystic swellings. The approach of surgery depends on the location of thelesion in relation to the mylohyoid and geniohyoid muscles. For larger cysts some prefer aspiration of the contents of the cysts before excising, it as it considerably decreases the size of the incision and provides better healing and thus better cosmetic results.

Key words: Cysts, Dermoid cysts, Intraoral lesions, Ranula

INTRODUCTION

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Congenital cystic swellings are classified into dermoid cysts, congenital ductal cysts, and branchial cleft anomalies like cystic hygroma. These cysts are usually composed of elements from all three germinal layers. Acquired cysts most common encountered are mucous retention cysts usually involving the minor salivary glands. The common sites of occurrence are the lips, buccal mucosa, and tongue. These true cysts with an epithelial lining result from duct obstruction. A simple ranula is a mucous retention cyst of the sublingual gland and was described as plunging when it extends from the floor of the mouth through

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the mylohyoid musculature into the neck. Mucoceles, in contrast, are not true cysts and do not contain an epithelial lining. Mucoceles represent mucous extravasation into the surrounding soft tissue.[1]

For early diagnosis, a detailed history with respect to onset, duration, size, site of the swelling, presence of any antecedent trauma. A high degree of suspicion is required on the part of the treating physician along with proper and meticulous clinical examination of the oral cavity. In our study, the clinical diagnosis was made on the basis of the clinical features in conjunction with fine-needle aspiration cytology (FNAC), conventional radiographs, ultrasonography (USG), and computed tomography (CT). Treatment includes intraoral surgical excision of the cyst, marsupialization of ranula, aspiration followed by transcervical excision.

MATERIALS AND METHODS

This retrospective and prospective study of 54 patients was conducted in the Department of Otorhinolaryngology and Head and Neck Surgery, Saraswathi Institute of Medical Sciences, Hapur, Uttar Pradesh, India from August 2010 to August 2014. A detailed history with respect to onset, duration, size, site of the swelling was taken. Proper and meticulous clinical examination of the oral cavity was done in all the cases. Clinical findings were confirmed by additional investigations like conventional radiographs, USG, CT/magnetic resonance imaging (CT/MRI), together with FNAC in some cases. USG was done to assess the nature of the contents of the swelling. CT/MRI was done in selected cases to know the exact location of the swelling and its relationship with surrounding important structures. FNAC was done for cytological evaluation of the swelling.

Observations

Out of the total 54 cases diagnosed with intraoral cystic lesions, 30 cases were male and 24 cases were female that showed a male:female ratio of 1.25:1. Age distribution of the patients ranged from18 months to 62 years.

In our study, it was found that 16 patients belonged to the age group of 18 months-15 years (29.6%), 20 between 16 and 30 years (37.1%), 12 between 31 and 45 years (22.2%), and six patients were between 46 and 62 years of age (11.1%) (Table 1).

The various symptoms with which the patients presented were noted. Intraoral swelling, pain in swelling, difficulty in eating food, extraoral extension were the common complaints encountered (Table 2 and Figure 1).

Out of the 54 cases, 16 were of Ranula, out of the 16 cases of ranula 10 cases were of simple ranula (18.5%) and 6 were of deep plunging ranula (11.1%), 6 cases were of dentigerous cyst (11.1%), 10 cases of dermoid cyst (18.5%), 2 parasitic cysts (3.7%), 14 cases were of mucus retention cyst (25.9%), and 6 were of cystic hygroma (11.1%) (Table 3 and Figure 2).

DISCUSSION

Intraoral cystic swellings are rare but not uncommon findings in ENT practice. The differential diagnosis of the swellings in the oral cavity ranges from ranula, Mucous retention cysts, dermoid and epidermoid cysts, cystic hygroma, lymphoepithelial cysts, palatal and gingival cysts, lymphangioma, pyogenic granuloma.[1]

Table 1: Agewise distribution of patients

Age group	Cases	Percentage
18 month-15 years	16	29.6
16-30 years	20	37.1
31-45 years	12	22.2
46-62 years	6	11.1

Table 2: Presenting symptoms of the patients

Symptom	Cases	Percentage
Intraoral swelling	54	100
Difficulty eating/swallowing	32	59.3
Pain in swelling	14	25.9
Extra oral extension	26	48.2

Table 3: Diagnosis of the various intra-oral swellings

Type	Cases	Percentage
Simple ranula	10	18.5
Plunging ranula	6	11.1
Dentigerous cyst	6	11.1
Dermoid cyst	10	18.5
Parasitic cyst	2	03.7
Mucus retention cyst	14	25.9
Cystic hygroma	6	11.1

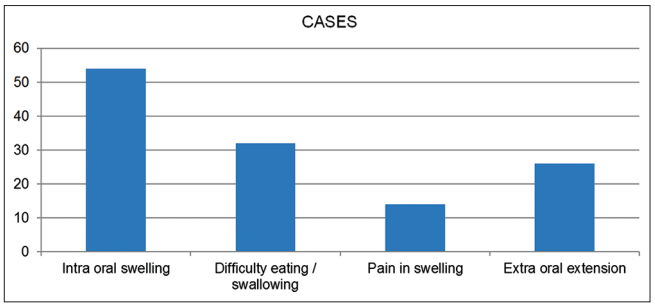

Figure 1: Presenting symptoms of the patients

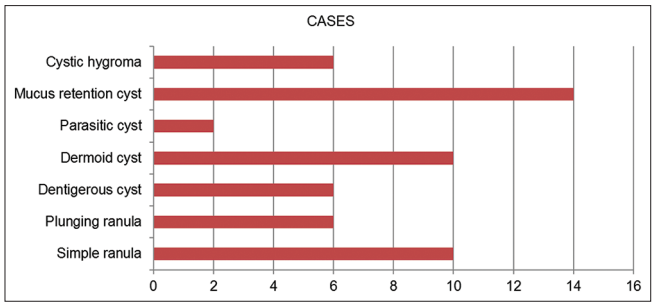

Figure 2: Diagnosis of the various intra-oral swellings

Ranulas are mucus extravasation cysts formed after trauma to the sublingual gland.[2] A ranula is called as plunging ranula when it extends from the floor of the mouth through the mylohyoid muscle and then into the neck.[3-5] The various methods for treatment of ranulas include marsupialization, excision of ranula, and laser excision and vaporization of the ranula.[2]

Dermoid cysts have been known to occur as a result of defective embryonic development (dysontogenetic). They represent cystic swellings that are filled with the keratinous sebum-like material. Dermoid cysts originating from the floor of the mouth comprise about 1.6-6.5% of all the dermoid cysts of the body and account for about 23-34% of head and neck dermoid cysts.[6,7] These can be congenital or acquired. The congenital dermoid cysts arise from embryonic cell rests of the 1st and 2nd branchial arch. The acquired dermoid cysts are caused due to trauma or due to iatrogenic causes. They result in occlusion of a sebaceous gland duct. It consists about 1.6-6.4% of the dermoid cysts of the body. On the basis of the anatomic location, the swellinds are divided into median genioglossal, median geniohyoid, and lateral cysts, while on the basis of histology they are divided into epidermoid, dermoid cysts and teratomas.[7]

Mucous retention cysts are usually found to involve the minor salivary glands and are usually seen on the lips, buccal mucosa, and tongue. True cysts are the ones with an epithelial lining and result from obstruction of the duct. A mucocele is formed secondary to rupture of an excretory duct of a salivary gland resulting in an outpouring of saliva into the surrounding tissues.[8] Mucoceles are not true cysts as they do not contain an epithelial lining. Mucoceles simply represent mucous extravasation into the surrounding soft tissue. The bluish discoloration is due to the vascular congestion and cyanosis of the tissue. This bluish discoloration also depends on the size of the lesion and proximity of lesion to the surface.[9] The management of these mucous retention cysts and mucoceles is by excision or marsupialization.[10]

Dentigerous cyst is defined as a developmental odontogenic cyst; they develop by an accumulation of fluid between the epithelium of the enamel and the tooth crown of an unerupted tooth.[11] It has been observed that 95% of dentigerous cysts involve the permanent dentition and about 5% cysts are found in association with supernumerary teeth. The age of presentation of dentigerous cyst associated with the supernumerary tooth is during the first four decades of life. Mesiodens is a supernumerary tooth situated between the maxillary central incisors. Mesiodens usually occurs unilaterally, but it may also be bilateral or rarely multiple.[12] Dentigerous cysts associated with the supernumerary teeth constitute 5-6% of all the dentigerous cysts while about 90% cysts are found in association with a maxillary mesiodens.[13]

Cystic hygromas are fluid-filled sacs resulting from blockage of the lymphatic duct system. Cystic hygromas can be single or multiple cysts found most common in the neck region. A cystic hygroma can be present at birth (congenital), or it may develop at any time A cystic hygroma in a developing baby can progress to hydrops (an excess amount of fluid in the body) and eventually fetal death. Some cases of congenital cystic hygromas resolve during the course of development. In other instances, it can progress in size to become larger in size. Cystic hygromas occur in 1% of fetuses during pregnancy.[14] In about 80% cases, the location of cystic hygromas is cervico-facial region. Approximately, 60% of cystic hygromas have onset at birth and about 90% become apparent before 2 years of age. Cystic hygromas can remain asymptomatic for the long duration. The indications of intervention include recurrent bouts of infection, respiratory distress, dysphagia, hemorrhage inside cystic hygroma, the sudden increase in the size of the lesion, lymph discharging sinus, and disfigurement.[15] Surgical excision of the cystic hygromas is considered as the treatment of choice. Extreme care should be taken to avoid perioperative complications. The possible complications following surgical excision varies from damage to the facial nerve, facial artery, carotid vessels, internal jugular vessels, thoracic duct and pleura, and incomplete excision in the case of infiltration to the surrounding structures. The various post-operative complications seen after the surgical excision of are wound infection, hemorrhage, hypertrophied scar, and lymphatic discharge from the wound.[16]

A thorough clinical examination is required on the part of the clinician, for early diagnosis a detailed history with respect to onset, duration, size, site of the swelling, presence of any antecedental trauma. High degree of suspicion on a part of the physician and proper and meticulous clinical examination of the oral cavity. Clinical findings need to be supported by investigations like conventional radiographs, USG, CT/MRI, together with FNAC.

Surgery is still the treatment of choice for intraoral cystic swellings. The approach of surgery depends on the surgical expertise of the surgeon and lesion's location in relation to the mylohyoid or geniohyoid muscles. Mostly the surgeons prefer that if the cyst is located over the mylohyoid, then surgery should be carried out through the intraoral approach, whereas if the cysts were under the geniohyoid muscle then extraoral incision, known as cervical approach should be preferred.[2] In the case of larger cysts some prefer aspiration of the contents of the cysts before excising it. In the case of an Intraoral approach, a midline vertical, or an elliptical incision on the floor of the mouth should be given first followed by blunt dissection; however, only small cysts can be enucleated using this kind of incisions as reported by other authors. Some surgeons prefer a bilateral incision along the mandibular crest, to obtain a good surgical approach and wider field to remove the cyst and to obtain adequate surgical control of the cysts located above the geniohyoid muscles.[4]

The extraoral approach or rather the cervical approach consists of a submental incision and a sharp, blunt dissection to reach the cystic lesion and thence to enucleate the lesion. The extraoral approach is preferred in the case of median geniohyoid or considerably larger sublingual cysts. The incision site is always closed in layers in extraoral approach and with intermittent interrupted sutures in intraoral approach to provide for drainage and avoid collection and thus providing better and cosmetically acceptable surgical results. A self-retaining and vaccumized Cervical Drain was kept in all the cases where large cysts were removed. The drain was removed post-operative on day 3. Specimens removed during surgery were sent for histopathological evaluation. The post-operative course did not present with any serious complication. Pain at the incision site, mucosal edema, collection at the site, hematoma were seen only in few post-operative cases. All the operated cases were followed for up to 10 months, and no recurrence was found during this period.

CONCLUSION

Cystic swellings occurring in the oral cavity are successfully diagnosed and managed by a combined intra- and extraoral surgical approach. It follows a systemic approach consisting of detailed history, clinical examination and appropriate imaging techniques. FNAC of the mass is diagnostic in a large number of cases. Differential diagnosis of such lesions includes Ranula, Mucous retention cysts, dermoid and epidermoid cysts, cystic hygroma, lymphoepithelial cysts, palatal and gingival cysts, lymphangioma, pyogenic granuloma and embryonic abnormalities. Surgery is still considered as the treatment of choice for intraoral cystic swellings. However, the approach of surgery depends on the location of the lesion with respect to the mylohyoid or geniohyoid muscles. Most of the surgeons prefer to remove the cyst through intraoral approach if the cyst is located over the mylohyoid muscle. Whereas the extraoral incision also known as the cervical approach is to be preferred when the cysts are located under the geniohyoid muscle.

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Original Article

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Dimorphism of Canine: A Diagnostic Value in Gender Identification - A Clinical Study

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Abstract

Introduction: Forensic odontology plays a decisive role in establishing the sex of victims with bodies mutilated beyond recognition due to major mass disaster. Teeth are the most indestructible part after the death of all parts of the body. Teeth are readily accessible for examination and do not need special dissection. Hence, teeth provide excellent material in living and not living populations for anthropological, genetic, ontological, and forensic investigations. Among all the teeth, the canines are found to exhibit greatest sexual dimorphism. Permanent canines and their inter-arch widths are known to contribute to sex identification in identification through dimorphism.

Purpose: The purpose of present study was to assess whether dimorphism of permanent maxillary and mandibular canines, as well as inter-canine distance, play a role in establishing gender identification.

Materials and Methods: The present study involved 100 subjects, 50 male and 50 female patients. Mesiodistal widths of the four canines and interarch distance between the maxillary and mandibular canines were measured on the dental casts of each of the subjects. A mean value of the canine index was calculated for both genders. This value was used to calculate the standard maxillary and mandibular canine index.

Result: All measurements showed statistically significant sexual dimorphism. Inter canine arch width and mesiodistal crown widths of canine were less in female than male. Conclusion: Canine plays an important role in gender identification. This study establishes dimorphism of the canine as a diagnostic value in gender identification.

Key words: Arch width, Canines, Forensic odontology, Gender, Intercanine distance

INTRODUCTION

The identification of a dead body may be required in cases of sudden and unexpected death, fires, explosions, and railway or aircraft accidents, mutilated or hidden decomposed bodies.[1] Sex determination of skeletal remains is an important part of archeological and many medico-legal examinations, particularly where the bodies are damaged beyond recognition. Teeth are excellent material for anthropological, genetic, and odontologic investigations in both living and dead population and are therefore of paramount importance in forensic practice. Forensic dentists can use this data to provide significant conclusions to medical examiners and detective.[2] This is because the unique traits and characteristics of teeth and jaws. The study of teeth reveals a lot concerning forensic medicine. In particular, it is useful in human identification. Forensic Odontology tells us a lot about the determination of age from various methods. In addition to the determination of age, sex can also be determined from the teeth. Determination of sex using skeletal remains presents a great problem to forensic experts, especially when only fragments of the body, are recovered. Forensic dentists can assist other experts to determine sex of the remains by using teeth and skull.[3]

Various features of teeth, like morphology, crown size, root lengths, etc., are characteristic for male and female

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sexes. There are also differences in the skull patterns. These will help a forensic odontologist to identify the sex.[4] Very few studies have been carried out to know dimorphism of permanent maxillary and mandibular canines play a role in establishing gender identity. Hence, this study was carried out to establish dimorphism of permanent maxillary and mandibular canines, as well as intercanine distance play a role in establishing gender identity. It was also planned to investigate the effect of "gender factor" on the morphometry of maxillary and mandibular canines.

MATERIALS AND METHODS

The present study involved 100 subjects, 50 male and 50 female patients, ranging between 14 and 20 years of age, who came to the Department of Oral Medicine and Radiology were included in the study. Inclusion criteria of this study was healthy gingiva and periodontium, caries-free teeth, normal overjet and overbite, absence of spacing in anterior teeth, whereas exclusion criteria of study was presence of partially erupted teeth, patient with dental/occlusion abnormalities and teeth showing physiologic or pathologic wear and tear, patients with deleterious oral habits. Information was given to all the participants regarding the need and design of the study, and the need for undergoing a clinical examination and making an impression. Informed consent was taken from all the patients. The study was approved by the Ethical Committee.

Impressions of upper and lower arch make with the help of alginate to all the patients, then cast of the immersion made by the help of dental stone (Figures 1-5). Measurements of mesiodistal widths of the four canines and interarch distance between the maxillary and mandibular canines were made on the dental casts of each of the subjects with the help of Vernier caliper with a resolution of 0.1 mm and divider (Figures 6 and 7). The data were coded on Microsoft excel sheet and analyzed using SPSS statistical package version 17. Statistical analysis was done by student *t*-test.

RESULTS

It was observed that the mean mesiodistal dimension of right side maxillary canine were greater in males than females, i.e., 0.73 ± 0.07 in males and 0.54 ± 0.05 in females. Furthermore, the mean mesiodistal dimensions of left side maxillary canine were greater in males, i.e., 0.72 ± 0.07 in males and 0.54 ± 0.05 in females. Same results were observed of the right side mandibular mean mesiodistal dimension of canine 0.65 ± 0.06 in males and 0.50 ± 0.04 in females, whereas mean mesiodistal dimension of left side mandibular canine 0.66 ± 0.06 in males and 0.50 ± 0.05 in female, which were again greater in males than females.

Figure 1: Armamentarium for examination, making impressions and obtaining study casts

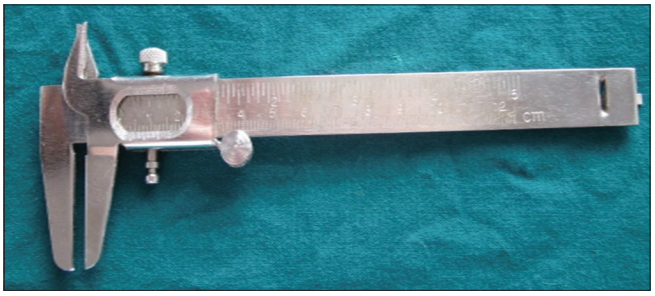

Figure 2: Vernier caliper for measurements on the study casts

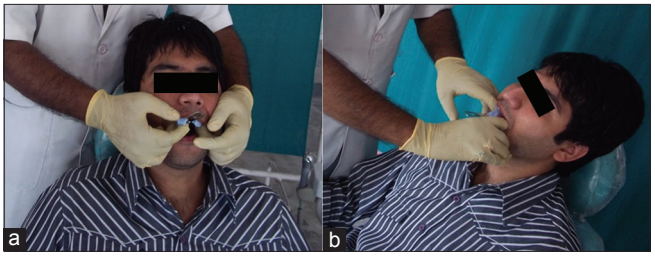

Figure 3: (a) Impression making for the maxillary arch, (b) impression making for the mandibular arch

Figure 4: Impression trays

However, mean intercanine distance in maxilla 3.38 ± 0.53 in males and 2.99 ± 0.16 in females, whereas mean intercanine distance in mandible 2.77 ± 0.26 in males and 2.48 ± 0.10 in females which were also greater in males than females. *P* value is highly significant $P < 0.001$ (Figure 8).

DISCUSSION

Identification of sex from adult human skeletal remains is the most reliable if the complete skeleton is available for analysis.[5,6] A basic problems in physical and forensic anthropology is determination of the sex of incomplete and fragmentary skeletal remains.[7] Teeth are the strongest structures in the human body and are known to resist postmortem destruction. They are usually retained in skeletal specimens and hence, can be used in sex differentiation.[8]

Canines are used because of their durability in the oral cavity. These are the least frequently extracted teeth because decreased incidence of caries and periodontal disease. Canines are reported to withstand extreme conditions and have been recovered from human remain even in air disasters and hurricanes.[9-11]

This study was carried out to analyze the sexual dimorphism in the maxillary and mandibular canine and the intercanine arch width. In our study, we have selected the age group of 14-20 years of age because intercanine distance do not increase after 12 years of age and after 20 years of age regressive alteration take place which were comparability with previous studies on canine indices.[12,13]

The methods of measurement of canine width in the present study were done with a universal method and in agreement with a number of studies when the anatomic point of measurement on the tooth is considered.[14,15] To obtain a statistically relevant interpretation with consideration to the study period, a sample size of 100 subjects comprising of 50 males and 50 females was decided which was in accordance to a study conducted by Boaz and Gupta.[10]

In this study, the statistical mean of maxillary right canine left canine and mandibular right and left canine of males were found to have larger mesiodistally than females. P value finding is high ($P < 0.001$), indicating a high sexual dimorphism. These results were consistent with the results of study conducted by Kaushal *et al.*[9]

In our study, mean intercanine distance in maxilla 3.38 ± 0.53 in males and 2.99 ± 0.16 in females, whereas mean intercanine distance in mandible 2.77 ± 0.26 in males and 2.48 ± 0.10 in females which were also greater in males than females. *P* value is highly significant $P < 0.001$. The results were coinciding with the results of study conducted by Rao *et al.*[13]

Figure 5: Casts

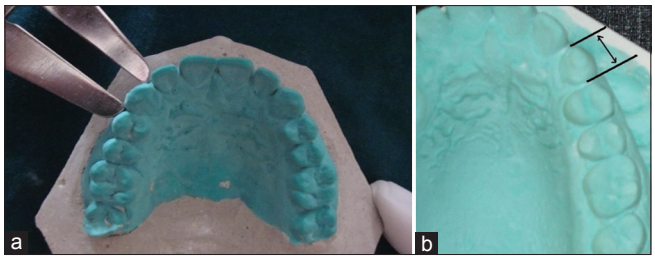

Figure 6: (a) Measurement of mesiodistal width of canines on study casts, (b) measurement of mesiodistal width of canines on study casts

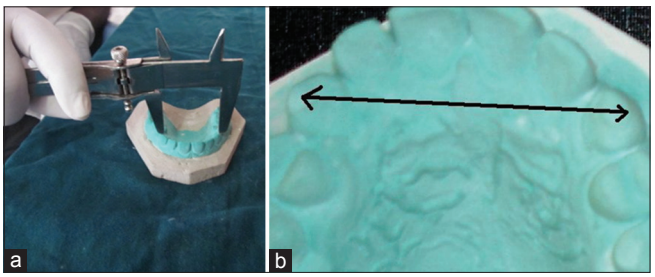

Figure 7: (a) Measurement of intercanine arch width on study casts, (b) measurement of intercanine arch width on study casts

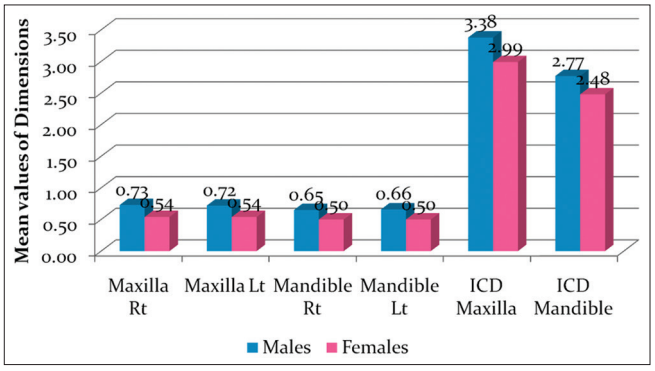

Figure 8: Comparison of various dimensions in different genders

Main drawback of our study was that the sample size was small. Further dimorphic studies of canine are advised with larger samples size of so that the incidence of sexual dimorphism of canine could be strongly established in future.

CONCLUSION

Forensic odontology is an emerging field which requires easy and inexpensive means of identification of persons from fragmented jaws and dental remains. In future, a database should be established of dental morphometric measurements to determine gender for anthropological, legal, and forensic purpose. Canine is a key tooth for gender identification and is diagnostic value in forensic odontology.

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Original Article

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Tennis Elbow Treatment with Platelet Rich Plasma: A Prospective Study

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Abstract

Introduction: Tennis elbow treatment is still remains a difficult task; the use of platelet-rich plasma (PRP) is a proactive therapeutic option that jump starts the healing process, which contains several different growth factors and other cytokines that stimulate healing of bone and soft tissue.

Materials and Methods: This is a prospective study of 50 patients, done at Osmania General Hospital, Hyderabad, India, for 2 years. The primary analysis included visual analog scale pain scale, for measuring pain in patients, local tenderness, pain on extension of the wrist, grip strength, elbow swelling were clinically assessed at different interval of follow-up, clinical and functional outcome were evaluated at final follow-up with statistics.

Results: Results were calculated based on descriptive statistics with SPSS version 19. The average follow-up was 1.5 years. Results were excellent in 40, good in 6, fair in 1 and poor in 3. In two cases, there was superficial infection seen; in one nerve palsy; in three subjects pain worsened; and ended up in surgical intervention.

Conclusion: Treatment with PRP holds promising results with minimal risk for the treatment of Tennis elbow. A more scientific evidence studies need to done before we can determine whether PRP therapy is effective in other conditions. PRP therapy as a viable procedure that may decrease the progression of more injuries may decrease the overall time for healing, and therefore, may setback the overall need for surgical intervention.

Key words: Platelet-rich plasma, Tennis elbow, Visual analog scale

INTRODUCTION

Tennis elbow is due to cumulative microtrauma from repetitive wrist extension and alternating pronosupination of forearm with angiofibroblastic degeneration of the common extensororigin.[1] Ultrasound therapy, extracorporeal shock wave therapy, laser therapy, autologous blood injection, and platelet-rich plasma (PRP) have been in use for tennis elbow treatment. Tennis elbow treatment is still unsolved; the use of PRP is a proactive therapeutic option which jumpstarts the healing process, which contains several different growth factors and other cytokines that stimulate healing of bone and soft tissue.[2] In the current study, we report long-term follow-up of tennis elbow treated with PRP and analyze the efficacy.

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MATERIALS AND METHODS

The study was conducted at Osmania General Hospital, Hyderabad. Patients between 20 and 50 years of age who had positive clinical tests (Thomson's and Cozen's test) were included in the study. Patients with arthritis of elbow, cervical spine pathology, infection, myositis, previous elbow trauma, previous steroid injection, or surgical intervention were excluded from this study. About 30 ml of the patient's blood was collected.[3] The blood sample is placed in a centrifuge to separate the PRP from the other components of whole blood. PRP was injected into the site of the maximum tenderness. Patients were asked to rate their pain according to visual analog scale (VAS). All cases were protected with brace initially and given anti-inflammatory agents for 1 week with cold fomentation, and then restoration of normal daily activities were allowed from the 3rd week with stretching and physiotherapy.[4]

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The primary analysis included VAS[5] for measuring pain in patients, local tenderness, pain on extension of the wrist, grip strength, elbow swelling were clinically assessed at different interval of follow-up, clinical and functional outcome were evaluated at final follow-up with statistical analysis. Patients were assessed after 1 week, 3 weeks, 2 months, 4 months, 6 months, and 12 months. Results were calculated based on descriptive statistics with SPSS version 19.

RESULTS

This series consisted of 50 patients of whom 32 were males and 18 were females with age range from 20 to 50 years (Figures 1 and 2). The average follow-up was 1.5 years. Results were excellent in 40, good in 6, fair in 1 and poor in 3. In two cases, there was superficial infection seen but subsided with oral antibiotics and did not require any surgical intervention; in one case nerve palsy which eventually recovered fully without any intervention; in three cases pain worsened and landed up in surgical intervention and subsequent pain relief. The mean VAS decreased continuously and significantly up to 9 months (Figure 3).

DISCUSSION

Tennis elbow is a frequent cause of disability. There are many treatment options available, suggesting no single procedure is effective in this condition. Common treatment is physiotherapy, immobilization, and steroid injection.[6] This treatment is with a high frequency of relapse and recurrence. This is due to intralesional steroid injection leads to permanent changes within the structure of the tendon and due to overuse of the arm after injection as a result of direct pain relief.[7] Ultrasound therapy also has gained popularity. In a short-term study, using whole blood, Edward, and Calandruccio[7] reported 78% good results in treating tennis elbow with the requirement of multiple injections.

The use of PRP is a proactive therapeutic option which jumpstarts the healing process, which contains several different growth factors and other cytokines that stimulate healing of bone and soft tissue.[8,9] Klein *et al.*[10] supported this thought with *in vitro* data, reporting transforming growth factor beta significantly increases Type I collagen production in tendon sheath fibroblasts. In other study for chronic elbow tendinosis PRP injection showed 93% excellent results when compared to pre-injection status.[11]

The PRP has got potential to regenerate bone and soft tissue function and details of which is still a mystery. PRP

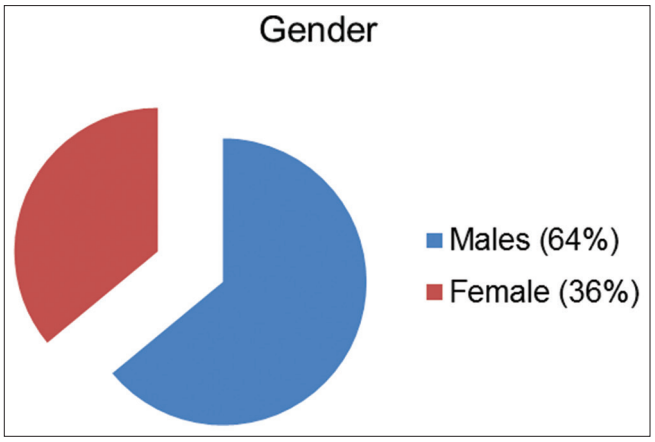

Figure 1: Depicting gender distribution in this series

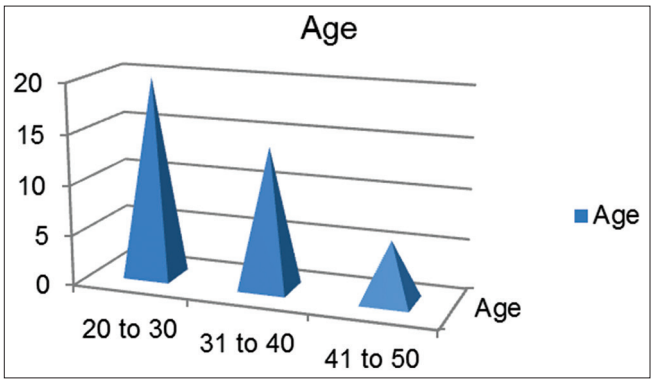

Figure 2: Depicting age distribution in this series

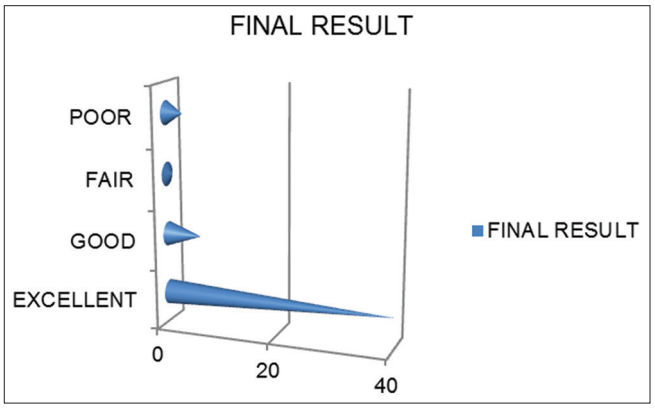

Figure 3: Depicting final result in this series

after injecting to the pathological site gets activated by collagen from the surrounding soft tissue, releasing growth factors, and cytokines.[12] These bioactive proteins and amino acid chains in turn stimulate local stem cells and enhance extracellular matrix gene expression, following which reparative cells from the vascular tissues and bone marrow then occurs. PRP has the potential to inhibit inflammation, apoptosis, and metalloproteinase activity. This results in restoration of soft tissue and structural component, which can withstand stress and strain, hence a reduction in pain.

The molecular afferent or efferent receptors are altered with PRP and modulation occurs in the microvascular level of soft tissues.[13] Further, more detailed study needs to be done to know the exact action pathway of PRP.

In this study mean VAS scale decreased statistically up to 9 months except immediate and 1 week ($P < 0.05$). It was observed the pain was a higher post injection and later started decreasing drastically further.

CONCLUSION

Treatment with PRP holds promising results with minimal risk for the treatment of Tennis elbow. More scientific evidence studies need to done before we can determine whether PRP therapy is effective in other conditions. PRP therapy as a viable procedure that may decrease the progression of more injuries may decrease the overall time for healing, and therefore may setback the overall need for surgical intervention.

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Original Article

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A Study of Neoplastic Lesions of Colorectum in a Tertiary Care Hospital

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Abstract

Background: Intestinal tumors account for a large proportion of all neoplasm. Colorectal cancer is the third most common cancer in men and the second in women worldwide, with significant geographical, racial and ethnic variation in its incidence rate and pattern.

Aims and Objectives: (1) To study the occurrence of neoplastic lesions of colorectum during a period of 1-year, (2) to evaluate different histopathological types of tumors of colorectum and staging them based on histopathological examination and clinical correlation, (3) to correlate the various neoplastic types of colorectum in relation to age, sex, family history, and dietary habits of the patient, (4) to compare the various histologic types with data available from other parts of India and also western countries.

Materials and Methods: The material consist of 120 specimens which consist of resected specimens and biopsies of neoplastic lesions of colorectum received in Department of Histopathology in Gauhati Medical College were analyzed with clinical and gross details and histopathological findings. The duration of study is 1 year from April 2014 to March 2015.

Results: Out of 120 specimens received, 61% were resected specimens and 39% were biopsy specimens. Lesions were further divided into benign and malignant lesions. Malignant lesions were a more common than benign lesions. Benign lesions were common in younger age, whereas malignant lesions were commonly seen in the elderly. Age group varies from 4 to 88 years. The majority of cases were seen in the 7th decade of life followed by the 6th decade. Males (66%) were more common affected than females (34%) and male:female ratio was 1.9:1. Overall, adenocarcinoma was the most common neoplastic lesions. Adenoma was the most common polypoidal lesion.

Conclusion: Malignant neoplasm is a more common than benign neoplasm in the colon. The most common neoplastic lesion is the adenocarcinoma of colon.

Key words: Adenocarcinoma, Adenoma, Colon, Neoplasm, Polyp

INTRODUCION

Colorectal cancer (CRC) account for a large proportion of all neoplasm. Epithelial tumors of the colorectum are a major cause of morbidity and mortality worldwide. In general, cancer incidence and mortality rates have been higher in economically advantaged countries.[1]

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CRC is the third most common cancer in men and the second in women worldwide.[2] Cancer of the colon is not a very common disease in our country and the incidence is much lower than in the western world. The incidence in India is about 7/100,000.[3] A great majority (98%) of all cancers in the colorectum are adenocarcinomas. The cause and pathogenesis of colorectal carcinoma are related to both environmental and genetic factors. The most obvious genetic factor is the high predisposition for colorectal carcinoma in patients with familial adenomatous polyposis (nearly 100% by age 50 years).

Overall, about 80% of colonic polyps are adenomatous in type.[4] Hyperplastic and juvenile polyps are the other common forms.

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MATERIALS AND METHODS

This is a cross-sectional observational study. The duration of study is 1 year from April 2014 to March 2015. It was carried out in the Department of Pathology, Gauhati Medical College and Hospital, Guwahati. The ethical approval was taken from the Srimanta Sankardeva University of health sciences Ethical Review Committee. The material for the study consists of resected specimens and biopsies of neoplastic lesions of colorectum. Biopsies of adequate size and from the representative sites were included in the study. Similarly, inadequate biopsies were excluded from the study.

The biopsy specimen obtained in the Department of Pathology was fixed in 10% buffered formalin. Formalin fixed specimens were subjected to detailed gross examination and subjected for histopathological processing and paraffin blocks prepared. Sections were cut at 3-5 μ thickness and stained by hematoxylin and eosin and mounted in DPX. Immunohistochemistry was done in selected case to confirm the diagnosis. The slides thus prepared were then examined under the microscope, and the lesions were diagnosed and classified according to the recent WHO classification.

RESULTS

A total of 120 cases were received out of which 31 cases (25.8%) showed benign tumors and 89 cases (74.2%) were diagnosed to have malignant tumors. A total number of resected specimens were 73 (60.9%) and biopsy specimens were 47 (39.1%). Among the resected specimens 58 were colectomy specimens and 15 were polypectomy. The age ranged from 4 to 88 years (Table 1). Out of these 79 (65.9%) were males and 41 (34.1%) were females.

Malignant Tumors of Colorectum

Age range of malignant tumor was in the range of 15-88 years with a mean age of 56 years (Table 2). A maximum number of tumors were observed between 61 and 70 years of age.

Majority of the patients with CRC were non-vegetarian. Most of the patients consumed bakery items regularly. 20 (22.5%) out of 89 patients has family history of CRC.

Rectum was the common location involved with 23 (25.8%) cases of the total 89 carcinoma of colorectum followed by sigmoid colon with 20 (22.5%) cases. (Table 3)

The most common morphology of tumor was ulceroproliferative, followed by annular type (Figure 1).

Table 1: Age incidence of all 120 cases of neoplastic lesions in present study

Age in years	Number of cases	Percentage
0-10	12	10.0
11-20	5	4.2
21-30	6	5.0
31-40	11	9.1
41-50	17	14.2
51-60	27	22.5
61-70	30	25.0
71-80	9	7.5
81-90	3	2.5
Total	120	100

Table 2: Age and sex incidence of colorectal carcinomas

Age in years	Male	Female	Total
11-20	1	1	2
21-30	3	2	5
31-40	3	1	4
41-50	9	4	13
51-60	15	9	24
61-70	19	11	30
71-80	5	3	8
81-90	2	1	3
Total	57	32	89

Table 3: Location of the tumors of colorectum

Location	Total	Percentage
Caecum	1	1.1
Ascending colon	9	10.1
Transverse colon	10	11.2
Descending colon	8	9.0
Sigmoid colon	20	22.5
Rectosigmoid junction	18	20.2
Rectum	23	25.8
Total	89	100

Table 4: Dukes staging

Dukes stage	Number of cases	Percentage
A	20	34.4
B	22	38.0
C	12	20.6
D	4	7.0
Total	58	100

Patient with lesions in proximal colon mainly presented with pain abdomen, mass per abdomen and anemia. Patients with more distal lesions presented with altered bowel habits, spurious morning diarrhea, and constipation. Patients with rectal lesions mainly presented with bleeding per rectum and mass per rectum.

Of the 89 malignant lesions, 86 were adenocarcinoma, constituting 96.6% of the colon. Two cases were malignant

Table 5: TNM staging

TNM stage	Number of cases	Percentage
O	0	0
I		
A	6	10.3
B	14	24.1
II		
A	22	38.0
B	0	0
III		
A	7	12.0
B	5	8.6
IV	4	7.0
Total	58	100

TNM: Tumor, Nodes and Metastasis

gastrointestinal stromal tumor (GIST) and a single case of non-Hodgkin lymphoma of diffuse large B-cell lymphoma (DLBCL) was found. Immunohistochemistry with CD117 for GIST and CD19 and CD20 were done for DLBCL to confirm the diagnosis.

Histologicaly adenocarcinoma was divided into three groups, based on mucin production and signet ring cell into adenocarcinoma, mucinous adenocarcinoma and signet ring cell carcinoma. In our study total 73 adenocarcinoma, 8 mucinous adenocarcinoma, and 5 signet ring cell carcinoma were encountered. (Figures 2 and 3)

Non mucinous adenocarcinoma was divided into four grades based on degree of differentiation of tumor. Well differentiated adenocarcinoma (38), moderately differentiated adenocarcinoma (26), poorly differentiated adenocarcinoma (9), and undifferentiated adenocarcinoma (0).

Distant metastasis was observed in four cases. Three cases have distant metastasis to liver and 1 has metastasis to liver and lung. Both Dukes staging (Table 4) and Tumor, Nodes and Metastasis (TNM) staging was done for resected specimens of colon.

Polyps of Colorectum

Total 31 polypoidal lesions were encountered in colorectum. Out of 31, 30 were benign, and 1 adenocarcinoma was found to arise in an adenomatous polyp. A maximum number of polypoidal lesions encountered was adenomas, total 20 (64.5%) in numbers. The other polypoidal lesion was juvenile polyp, total 11 (35.5%) in numbers. Among the adenomas 17 (85.0%) were tubular and 3 (15.0%) were villous. Maximum number of cases was seen in age group of 0-10 years. The majority of patients had clinical history of bleeding per rectum.

Majority of the polyps were located in rectum 20 (64.5%) followed by sigmoid colon 8 (25.8%) and descending colon 3 (9.7%).

Figure 1: An annular type of growth in large bowel (adenocarcinoma)

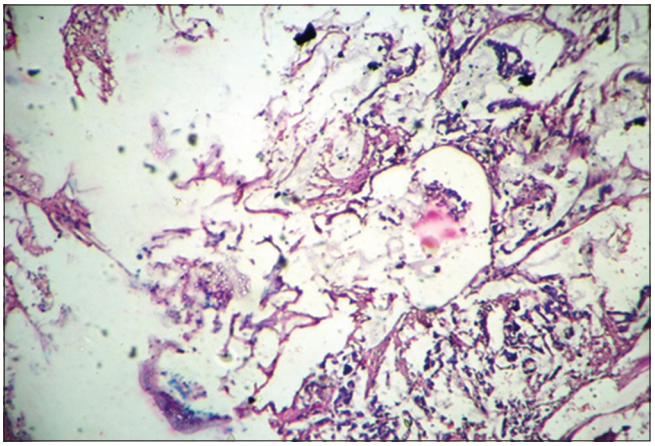

Figure 2: Mucinous adenocarcinoma (H and E, ×10)

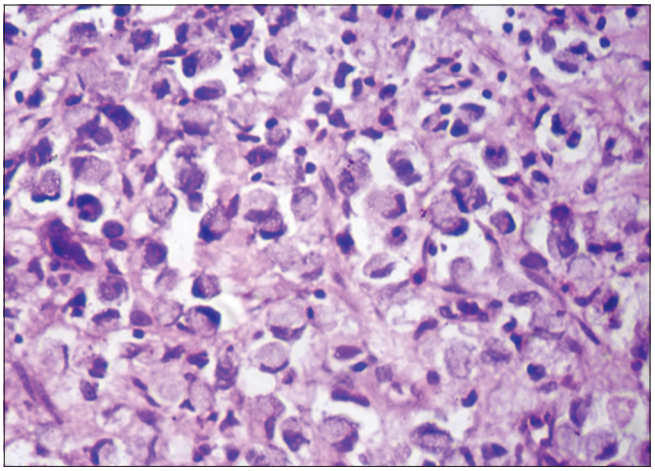

Figure 3: Signet ring cell carcinoma (H and E, ×40)

DISCUSSION

Peak age of incidence of colorectal carcinoma is 61-70 years. Around 27% cases of cancer occur before the age 50.

The risk of CRC increases significantly after the age of 50 years. Age range of malignant tumor was in the range of 15-88 years with a mean age of 56 years. Dakubo *et al.* 2014[5] and Fazeli *et al.* 2007[6] got similar results. The present study shows a higher incidence of malignant lesions than benign lesions. The study shows male preponderance which is compared with other Indian study.[7] Most of the patients in our study were non-vegetarian taking meat frequently. Most colorectal tumors are located in distal colon, mainly in sigmoid colon and rectum, but there is evidence of change in pattern of distribution in recent years, with an increasing proportion of more proximal carcinomas.[8] Ul-Rasool *et al.*,[9] Hamid *et al.*[10] and Abdulkareem *et al.*[11] has similar findings with the present study. Adenocarcinoma was the most common type of malignancy accounting for 96.6% of malignancy which is consistent with findings of other studies.[7,9,11,12] Histological grading of adenocarcinoma varies in different studies. Hamid *et al.*,[10] Abdulkareem *et al.*[11] and the present studies got higher percentages of well differentiated adenocarcinoma where as some got higher percentages of moderately differentiated adenocarcinoma.[9,12] Most of the cases presented in TNM Stage II and only few in TNM Stage IV (Table 5).

The present study shows majority of adenomatous polyps followed by juvenile polyp. The finding is close to Chitale,[13] 2000. No hyperplastic polyp was encountered in the study due to lower number of cases studied. There is higher incidence of tubular adenomas and most of them are pedunculated. Majority of the polyps were located in rectum which is consistent with Jose Tony *et al.* 2007.[14]

CONCLUSION

From the present study it can be concluded that the malignant lesions are more common than the benign lesions in colorectum. Males are the predominantly affected both in benign and malignant lesions. The most common neoplastic lesion is the adenocarcinoma of colon which was seen commonly in 7th decade of life. The most common location was found to be in rectum. The age and sex prevalence, as well as histopathological characteristics, are similar to findings from other parts of the world. -Family history, alcohol, smoking and red meat are the major risk factors associated with intestinal malignancies. The most common polyp found to be adenomatous polyp followed by juvenile polyp which was commonly seen in young age. The most common location was rectum.

The present study has shown malignant lesions of the intestine in many young aged persons. So, any adult with complaints of vague abdominal pain, blood or mucus in the stool or features of hemorrhoids which may herald the onset of CRC should be adequately investigated with digital rectal examination and proctosigmoidoscopy, barium enema and other radiological investigation where appropriate.

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Original Article

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Effect of Preemptive Intravenous Paracetamol on Post-operative Analgesic Requirements in Patients Undergoing Laparoscopic Surgeries

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Abstract

Introduction: Preemptive analgesia has been defined as the treatment which starts before surgery to prevent the establishment of central sensitization of pain. Paracetamol is a safe, the well-tolerated drug with proven efficacy as the preemptive analgesic for moderate post-operative pain in laparoscopic surgeries.

Aim: To determine the effect of preemptive use of 1 g intravenous (IV) paracetamol on post-operative pain scores and analgesic requirements in patients undergoing laparoscopic surgeries under general anesthesia.

Materials and Methods: A total of 60 patients undergoing laparoscopic surgeries were randomized into two groups, who were given either an IV placebo or an IV injection of 1 g paracetamol, 15 min before induction. The post-operative pain relief was evaluated by a visual analog scale and consumption of tramadol as rescue analgesic in the post-operative period. The incidence of post-operative nausea and vomiting (PONV) and any other complications were also measured in the post-operative period.

Results: At 15 min and 30 min, mean pain scores of "Group NS" were significantly more than those of "Group P" ($P < 0.05$). At 1, 2, and 6 h, mean pain scores of the two groups were comparable and statistically not significant ($P < 0.05$). The requirement of tramadol as rescue analgesia in "Group NS" was significantly more than "Group P" ($P < 0.05$). The incidence of PONV in the "Group NS" was more than "Group P."

Conclusion: Preemptive administration of 1 g of IV paracetamol in patients undergoing laparoscopic surgeries provided satisfactory analgesia and decreased post-operative tramadol consumption.

Key words: Intravenous paracetamol, Intravenous tramadol, Pain after laparoscopic surgeries, Post-operative analgesia, Preemptive analgesia

INTRODUCTION

Pain is a public health issue throughout the world, and it is the major clinical, social, and economic problem.[1] Although laparoscopic surgery results in substantially less severe, and prolonged discomfort compared with the corresponding open procedure, post-operative pain is still considerable and needs to be treated to reduce post-operative complications and hospital stay.[2]

The most common using drugs in the treatment of post-operative pain are opioid and non-opioid analgesics. Drugs such as non-steroidal anti-inflammatory drugs (NSAIDs), paracetamol, cyclooxygenase-2 (COX-2) inhibitors, local anesthetics, and steroids are often used for their opioid-sparing action to reduce the opioid-related side effects and hasten recovery.[3,4]

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The primary mechanism of these analgesic drugs is to inhibit the COX and prostaglandin synthesis.[5] Paracetamol (acetaminophen; *N*-acetyl-p-aminophenol) is an acetanilide derivative, safe, the well-tolerated drug with proven efficacy the analgesic. Its clinical effects arise most likely from the central action, and intravenous (IV) administration provides rapid and predictable therapeutic plasma concentration. Paracetamol was introduced for IV administration in a unit-dose form, ready for infusion solution in 2002. The mechanism of action of paracetamol is through the inhibition of prostaglandins and activation of descending serotonergic inhibitory pathways.[6,7]

The aim of this study was to evaluate the analgesic efficacy of preemptive IV paracetamol for post-operative pain relief after laparoscopic surgeries.

MATERIALS AND METHODS

After Ethical Committee approval and written informed consent of all the patients, this study was conducted. Patients aged 18-60 years scheduled for laparoscopic surgeries and classified as American Association of Anesthetists (ASA) physical Status I or II were included. Patients those having contraindications to paracetamol (allergy, liver disease) or to NSAIDs (esophagogastroduodenal disease, renal insufficiency, and abnormal coagulation) and patients those on treatment by steroids, NSAIDs, or opioids before surgery were excluded. The patients were divided into two groups of 30 in each. After shifting into the operation theater, all standard monitoring equipment was connected, and the crystalloid infusion was started. The study drugs were given IV as slow infusion 30 min before induction in the pre-anesthetic room. In "Group P," patients received 1 g of IV paracetamol and in "Group NS," patients received 100 ml IV normal saline over 15 min.

All the patients were pre-oxygenated with 100% oxygen using Bain's circuit for 3 min. All the patients were induced with injection thiopentone 5 mg/kg IV, injection fentanyl 2 μg/kg IV, injection vecuronium 0.1 mg/kg IV, and trachea was intubated with appropriate size ETT. Following intubation, maintenance of general anesthesia was accomplished by providing isoflurane in 40/60 oxygen/nitrous oxide and, if required, 0.01 mg/kg vecuronium was administered. If the duration of surgery was more than 90 min, the cases were excluded from the study. Heart rate, noninvasive blood pressure, SpO_2 and end-tidal CO_2 were monitored throughout the procedure. Patients were extubated after reversal with glycopyrrolate (0.01 mg/kg) and neostigmine (0.05 mg/kg) and thorough suctioning.

In the post anesthesia care unit, post-operative pain score was measured by using visual analog scale (VAS) of "0" to "10" where "0" indicated no pain and "10" is the worst imaginable pain. Post-operative pain was observed at the intervals of 15 min, 30 min, 1 h, 2 h and 6 h. Injection tramadol 50 mg IV used as rescue analgesic was given if the VAS score was more than three.[4]

Statistical Analysis

The comparison between the two groups was done by student's unpaired *t*-test and Mann–Whitney test. A probability value ($P \leq 0.05$ was considered as statistically significant.

RESULTS

The demographic data reveals that both groups are comparable in age, weight, sex, and ASA grade (Table 1). There was no statistically significant difference in the duration of surgery (74.35 ± 13.34 in "Group P," whereas in "Group NS" was 71.61 ± 14.34) (Table 1). At 15 min and 30 min mean pain scores of "Group NS" were significantly more than those of "Group P" ($P < 0.05$) (Table 2 and Figure 1). At 1, 2, and 6 h, mean pain scores of the two groups were comparable and statistically not significant ($P < 0.05$) (Table 2 and Figure 1). The requirement of tramadol as a rescue analgesia in "Group NS" was significantly more than "Group P" ($P < 0.05$) (Table 3 and Figure 2). Post-operative nausea and vomiting (PONV) was shown in Table 4 and Figure 3.

DISCUSSION

In the present study, pain management was started prior to pain initiation on the basis of preemptive analgesia. The

Table 1: Comparison of demographic parameters between two groups

Parameters	*n*=30		*P* value
	Group P	Group NS	
Age (years)	32.54±11.01	34±10.67	0.60
Sex (female/male)	16/15	17/14	0.79
Weight (kg)	59.19±7.91	56.84±6.87	0.215
ASA (I/II)	28/3	28/3	1.00
Duration of surgery (min)	74.35±13.34	71.61±14.34	0.438

ASA: American association of anesthetists

Table 2: Comparison of mean pain scores (VAS) between two groups

Intervals	Group P	Group NS	*P* value
15 min	2.06±0.63	2.61±0.56	0.0006
30 min	2.35±1.17	3.84±1.55	0.0001
1st h	2.42±1.12	2.87±0.99	0.0989
2nd h	2.13±1.06	2.52±0.89	0.1219
6th h	2±0.52	2.52±0.89	0.0549

VAS: Visual analog scale

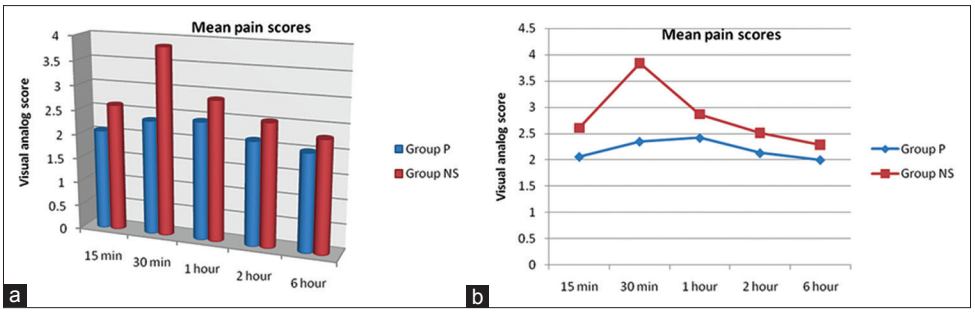

Figure 1: (a and b) Comparison of mean pain scores (visual analog scale) between two groups

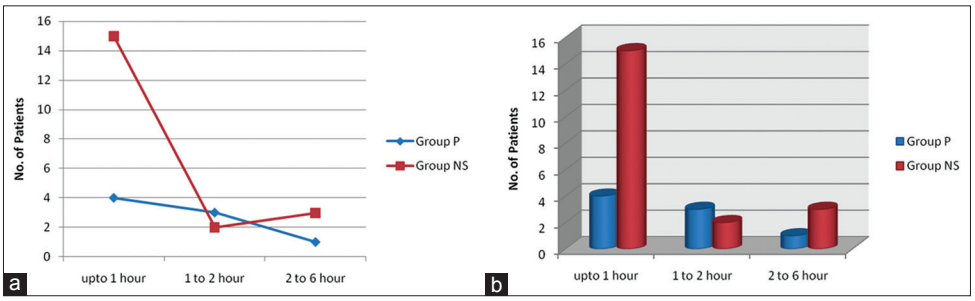

Figure 2: (a and b) Comparison of tramadol requirement between two groups

Table 3: Comparison of tramadol requirement between two groups

Duration	Number of patients (%) (*n*=30)		*P* value
	Group P	Group NS	
Up to 1 h	4 (12.90)	15 (48.39)	0.0002
1-2 h	3 (9.68)	2 (6.45)	0.64
2-6 h	1 (3.23)	3 (9.68)	0.301
Total	8 (25.81)	20 (64.52)	0.002

Table 4: Comparison of PONV between two groups

PONV	
Group P	Group NS
0	4

PONV: Post-operative nausea and vomiting

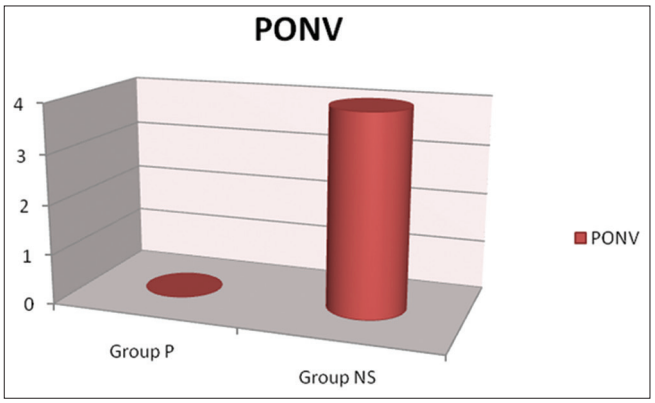

Figure 3: Comparison of post-operative nausea and vomiting between two groups

aim of preemptive analgesia, which has been investigated in recent years, is to provide analgesia prior to a painful stimulus to prevent central sensitization caused by the painful stimulus and, consequently, to decrease the need for post-operative analgesia.

Preemptive analgesia has been defined as treatment that: (1) Starts before surgery; (2) prevents the establishment of central sensitization caused by incisional injury and inflammatory injuries.

Paracetamol rapidly passes the blood-brain barrier, reaches a high concentration in the cerebrospinal fluid and has an anti-nociceptive effect mediated by the central nervous system (CNS).[8] This central effect has been regarded primarily as an indirect and reciprocal influence through COX enzyme inhibition, and probably through the serotoninergic system as well. Besides this central effect, it is accepted that paracetamol has a peripheral anti-inflammatory influence, although this effect is somewhat limited.[9]

Pre-emptive analgesia has the potential to be more effective than a similar analgesic treatment initiated after surgery. Consequently, immediate post-operative pain may be reduced, and the development of chronic pain may be prevented.[10]

In our study significant high mean pain scores were observed during post-operative period at 15 min and

30 min in "Group NS" (2.61 ± 0.56 and 3.84 ± 1.55, respectively) compared to "Group P" (2.06 ± 0.63 and 2.35 ± 1.17, respectively) (*P* - value 0.0006 and 0.0001, respectively). There was no significant difference in mean pain scores at 1, 2 and 6 h in both groups (*P*>0.05).

Choudhuri and Uppal *et al.*[11] Administered IV paracetamol 1 g as a pre-emptive analgesic in laparoscopic cholecystectomy and assessed its effects on intraoperative analgesic requirement, post-operative analgesic effectiveness, showed that IV paracetamol when used as pre-emptive analgesic just before induction as part of multimodal analgesic regime has significant opioid sparing effect, concluded that, no differences were observed between the two groups in the adequacy of analgesia as assessed by VAS scores. However, the median pain scores were significantly lower in the paracetamol group (Group P) at two intervals which are comparable with our study. This may be because of the initial loading dose of paracetamol providing a higher plasma concentration.

In a related study by Salihoglu *et al.*, preemptive use of 1 g IV paracetamol caused similar decrease in post-operative pain scores and requirement of rescue analgesia.[12] The similarly in another study Arici *et al.*, demonstrated significantly lower post-operative pain scores and consumption of rescue analgesia in patients who received 1 g IV preemptive paracetamol compared to patients who received normal saline.[13]

Clinical studies have also found that 1 g IV paracetamol employed alone is just as effective as 30 mg ketorolac, 75 mg diclofenac or 10 mg morphine.[14,15]

The requirement for rescue tramadol analgesia was in 25.8% of patients in the "Group P" compared to 64.5% of patients in "Group NS," which suggests that preemptive paracetamol group had less pain, high pain threshold or both. These results indicate that sufficient analgesic effectiveness was ensured in the post-operative period in Group I. In addition, the less values of the pain scores in the Group I may be explained by decreases in excitability in the CNS through blockade of nociceptive stimuli before damaging tissue architecture. We believe that since the preemptively delivered paracetamol prevents central sensitization; its analgesic effect continues longer than its effect period.

It is also demonstrated that the analgesic effect of IV paracetamol starts within 5 min, peaks at 1 h and lasts 4-6 h.[16]

Piguet *et al.*,[17] had demonstrated the close correlation between plasma concentration and analgesic effect of paracetamol with IV doses of up to 2 g in healthy volunteers.

Juhl *et al.*,[18] had demonstrated that the extent and duration of pain relief following third molar surgery was significantly improved after 2 g over 1 g of the initial IV dose of paracetamol.

In our study, we observed that four patients had PONV in Group NS, none of the patient had developed PONV in Group P, the related study done by Apfel *et al.*[19] concluded prophylactically administered IV Acetaminophen reduced PONV, mainly mediated through superior pain control.

CONCLUSION

To conclude, preemptive administration of 1 g of IV paracetamol in patients undergoing laparoscopic surgeries provided satisfactory analgesia and decreased post-operative tramadol consumption. Hence, 1 g of IV paracetamol can be safely administered preemptively for post-operative analgesia for laparoscopic surgeries.

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Original Article

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Prospective Analysis of Extracapsular Fractures of the Proximal Femur Treated with Proximal Femoral Nail

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Abstract

Introduction: Extracapsular fractures of the proximal femur occur as a result of high energy trauma in the younger population and in the elderly, due to a trivial fall in an osteoporotic bone. Most of the fractures are unstable and require anatomic reduction. Sliding compression screw systems have been in vogue for many years. However, in the recent years, intramedullary systems are gaining in popularity due to their several distinct advantages. The purpose of this study was to assess the outcome of these fractures treated with a proximal femoral nail (PFN).

Materials and Methods: The study group included 44 patients with intertrochanteric and subtrochanteric fractures. The fracture was reduced either by closed reduction or an open reduction. Each case was followed-up for a period of 2-year at periodic intervals. The Evans classification system was used for grading the fractures, and the Harris Hip score (HSS) was used to assess the functional outcome.

Results: The average age was 69 years. The average duration of the surgery was 55 min, and the blood loss was around 120 ml. The complication rate was minimal and included superficial infection, implant failure due to screw cut out and Z effect. Average duration for union was 16 weeks, and the fracture union rate was 98.5%. According to the HSS 75% achieved excellent results, and 20% showed good results and 5% exhibited poor results.

Conclusion: The PFN is an ideal implant in the treatment of suitable inter-trochanteric and subtrochanteric fractures. Its advantages include reduced operative time and blood loss, early return to daily activities, and a reduced complication rate.

Key words: Femur, Fracture, Intertrochanteric, Osteosynthesis, Subtrochanteric

INTRODUCTION

Extracapsular fractures (intertrochanteric and subtrochanteric fractures) of the proximal femur primarily involve the cortical and compact cancellous bone. Because of the complex stress configuration in this region and its nonhomogeneous osseous structure and geometry, fractures occur along the path of least resistance through the proximal femur.[1] Intertrochanteric fractures are the most common in elderly population accounting for 50% of total hip fractures, of which more than 50% are unstable.[2] The incidence has increased significantly in the recent years due to the advancing age of the population. In young individuals, the injury results from a high energy trauma, whereas in the elderly group, most of the fractures resulting from a trivial fall are because of osteoporosis.[3] Internal fixation is the treatment of choice for managing intertrochanteric fractures of the femur as most of these fractures are highly unstable. These are treated by various methods which include; the dynamic hip screw (DHS) - is the gold standard for intertrochanteric fractures.[4] Intramedullary devices such as the proximal femoral nail (PFN) are biomechanically stronger and more rigid compared to the extramedullary devices such as DHS. They allow earlier weight bearing and better rehabilitation. Therefore, the PFN has increasing popularity in the treatment of intertrochanteric fractures.[5]

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Purpose of the Study

The purpose of this study was to assess the outcome of inter and subtrochanteric fractures treated with PFN and to study the complications.

MATERIALS AND METHODS

44 consecutive patients with intertrochanteric and subtrochanteric fractures were considered for study in Sanjay Gandhi Institute of Trauma and Orthopedics, Bengaluru, Karnataka, India between August 2011 and November 2014. Inclusion criteria were patients older than 18 years, with closed inter-trochanteric fracture and subtrochanteric fractures, whereas exclusion criteria were age below 18 years and above 70 years, associated co-morbid conditions, and open and pathological fractures.

Pre-operative evaluation was done with local examination, assessment of associated injuries and general health and fitness for surgery. Standard radiographs like anteroposterior (AP) view of the pelvis with both hips lateral view of the injured hip, and a full-length AP and lateral view of the injured femur were obtained. Evans classification system was applied for evaluation of the fractures.

Operative Technique

All patients were positioned on the fracture table, and the fracture was reduced under fluoroscopy. If closed reduction failed, an open reduction was performed. Post-operative management included an immediate range of motion (ROM) exercises of the hip and knee joint along with toe touch walking on the 2nd post-operative day and weight bearing as tolerated by the patient in the non-comminuted fracture, whereas in a comminuted fracture, the patient was advised non-weight bearing mobilization for 3 weeks followed by partial weight bearing after confirming callous formation radiologically. Each case was followed-up for a period of 2 years and follow-up assessments were carried at 4 weeks, 8 weeks, 12 weeks, 6 months, and annually thereafter. The functional outcome was assessed with the Harris Hip score (HSS).[6] At each follow-up, ROM at the hip and knee joint, signs of infection local/deep, and any associated complaints were noted. Standard radiographs were taken to assess the position of the nail and screws, as well as callus formation, and any loss of reduction and angulation were noted.

RESULTS

Of the 44 patients, four were lost during follow-up and hence, excluded from the study. The average age was 69 years with a female preponderance (Figures 1 and 2).

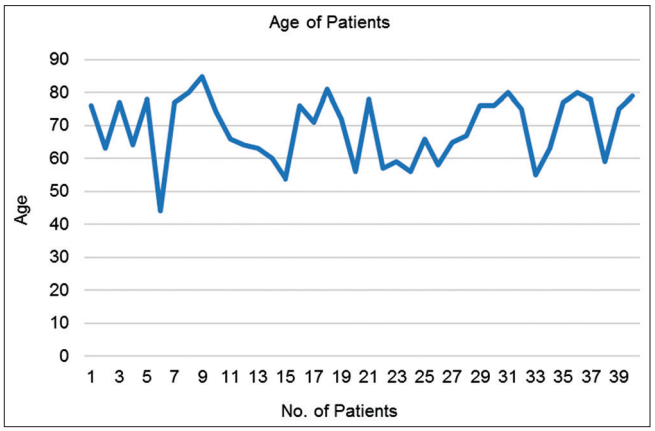

Figure 1: Distribution of patients based on age

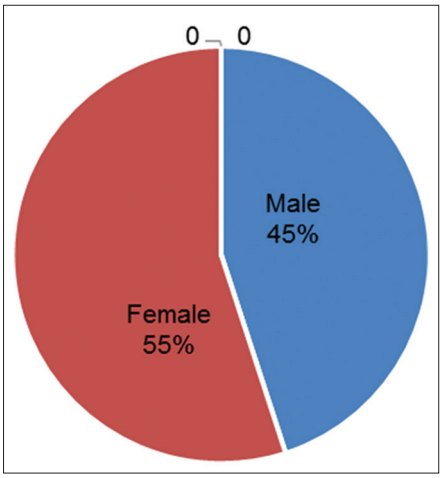

Figure 2: Sex distribution

The most common etiology was road traffic accident in younger patients and domestic fall in elderly patients. The average duration of the surgery was 55 min, and the blood loss was around 120 ml. The average incision size was 3 cm, and the average fluoroscopy time was 15 min. In four cases, as closed reduction was not achieved, an open reduction had to be performed. Superficial post-operative infection was seen in two cases which resolved with culture-specific antibiotics, and none of them developed deep infections requiring implant removal. Average duration for union was 16 weeks. One patient had implant failure due to Z affect which required revision surgery and bone grafting. During post-operative ambulation 20 cases (50%) gained pre-injury ambulatory status within 2 weeks, and another 20 cases (50%) gained in 8 weeks, and 4 cases had an abductor lurch. The HHS in 29 cases (72.5%) showed excellent results and seven cases (17.5%) showed good results, and two cases each (5%) showing fair and poor results (Figure 3).

DISCUSSION

PFN provides an intramedullary device inserted by means of a minimally invasive procedure which allows the surgeon

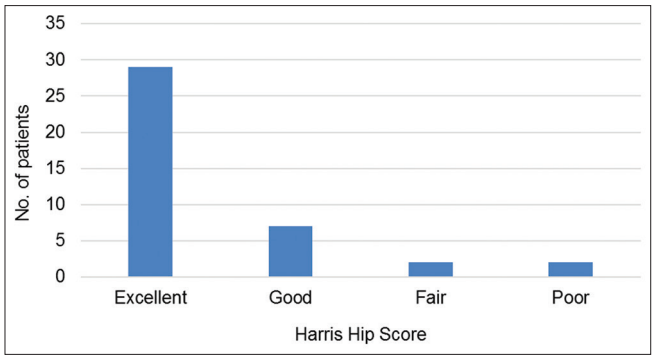

Figure 3: Distribution of cases based on Harris Hip score

to minimize soft tissue dissection, thereby reducing surgical trauma, blood loss and post-operative wound complications. It is best suited for the older patients.[7-9] Since the average age of the patient in the present series was 69 years, PFN is better implant to use for this age group.

The PFN itself serves as a buttress against lateral translation of the proximal fragment.[2] The intramedullary location of the junction between the nail and lag screw makes the implant stronger at resisting the binding force.[3] It has a reduced distance between the weight bearing axis and the implant leading to a shorter lever arm.[4] The PFN, like any other intramedullary device is a load sharing device, and bears the bending load which is transferred to the intramedullary nail and is resisted by its contact against the medullary canal.[5] The intramedullary hip screw is a more biological method of fixation. Götze *et al.*[10] compared the load bearing ability of osteosynthesis of unstable per- and subtrochanteric fractures and found that the PFN could bear the highest loads among all devices.

Friedl *et al.*[11] and Tyllianakis *et al.*[12] reported the need for open reduction in 8% and 6.66% cases in their respective series as closed reduction was not possible in a few unstable fractures. In this study, open reduction had to be performed in four cases (9%) as closed reduction was not achieved under fluoroscopy at the beginning of surgery.

Simmermacher *et al.*,[5] in a multicenter clinical study, reported technical failures of the PFN after poor reduction, malrotation or wrong choice of screws in 5% of the cases. A cut-out of the neck screw occurred in 0.6% cases. There was one case (4.4%) of implant failure in this study and reason for that was the occurrence of Z effect which required revision surgery. The Z effect refers to the movement of the hip pin toward the medial side into the hip joint with destruction of the cartilage of the joint. Menezes *et al.*[13] reported 3.45% of Z affect. Likewise, Boldin *et al.*[14] too reported a 7% failure rate.

The PFN has been shown to prevent femoral shaft fractures by having a smaller distal shaft diameter which reduces stress concentration at the tip.[5] However, Menezes *et al.*[13] reported 0.7% incidence of femoral shaft fractures. There were no cases of femoral shaft fracture in the current study.

The present study had a fracture union rate of 98.5%, and the results are similar to those of Tyllianakis *et al.*[12] and Boldin *et al.*[14] who had 97% and 100% union rates, respectively. The average operating time in this study was around 55 min, which is comparable to other studies. Pajarinen *et al.*[15] and Little *et al.*[16] reported operating times of 55 min and 54 min, respectively.

Pajarinen *et al.*[15] conducted a randomized study comparing the post-operative rehabilitation with the use of PFN and DHS, and concluded that PFN when used for trochanteric fracture have positive effect on speed of restoration of walking in comparison with DHS. During post-operative ambulation 20 of their cases (50%) gained pre-injury ambulatory status within 2 weeks, and another 20 cases (50%) gained in another 8 weeks; four cases had an abductor lurch. Kumar *et al.*[17] who compared the outcome of trochanteric fractures treated with DHS and PFN, had an average HSS of 97 in the PFN group at 2 years follow-up. In the present study, the average HSS was 91 at 2 years follow-up, and we had 72.5% excellent and 17.5% good results which are comparable to the results of Pajarinen *et al.* and Kumar *et al.* (Table 1).

Shortcomings of this study were a relatively lesser number of patients and a shorter follow-up. More comparative studies with other modalities of fixation are needed to establish the role of intramedullary devices in unstable intertrochanteric fractures of femur.

CONCLUSION

PFN is a useful device in the treatment of extracapsular fractures of the proximal femur (intertrochanteric and subtrochanteric fractures). It is a relatively easy procedure and a biomechanically stable construct which allows early weight bearing and helps in gaining pre-injury ambulatory status. The plate and screw device will weaken the bone mechanically. The common causes of fixation failure are instability of the fractures, osteoporosis, and the lack of anatomical reduction, failure of the fixation device and incorrect placement of the screw. At present, we consider that the PFN is a good minimally invasive implant for unstable proximal femoral fractures when closed reduction is possible.

In conclusion, the use of PFN for extracapsular fractures of the proximal femur has several distinct advantages, namely; lesser operative time with less operative blood loss, early return to daily activities, reduced complications like

Table 1: Comparison of few studies with our study

Name of the study	Number of cases	Implant used	Age	Blood loss (ml)	Operative time (min)	Complications
Pajarinen *et al.*	54	PFN	79	320	55	0
Little *et al.*	92	Holland Nail	83	78	54	5
Kumar *et al.*	25	PFN	63	100	55	0
Our series	40	PFN	69	120	48	3

PFN: Proximal femoral nail

infection, sliding, and limb length discrepancy. This study demonstrates that the PFN is more useful in unstable and reverse oblique patterns.

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Original Article

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High Heels Footwear Causes Heel Pain and Back Pain: Myth or Reality?

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Abstract

Introduction: Heeled footwear has been in use by women for centuries and has now become an integral part of the wardrobe not only in the west but also in India. Recent research suggests that up to one third of women suffer from permanent problems as a result of their prolonged wearing of heels. One in 10 women wear it at least for 3 days a week, and a recent survey found that one-third of them had permanent problems.

Purpose: Whether the high heel wear is the actual cause of back pain is not yet clear. Literatures vary in their results regarding the same. Hence, the present study was done to assess this cause and effect.

Methods: The study was conducted at the orthopedic outpatient department of a tertiary care hospital, from July 2014 to December 2014.100 female patients who were using heeled shoes and who volunteered to participate in the study were included. The heel height was measured using measuring tape and were classified into three groups (<2.5 cm, 2.5-5 cm, >5 cm). A Proforma with a questionnaire was given to all the participants and their response were noted.

Results: Out of the 100 female volunteers, who participated in the study, 44 had complaints of heel pain regardless of the heel height, 56 had back pain, and many had both heel pain and back pain complaints, based on the questionnaire evaluation. We were further able to distinguish both heel pain and back pain, based on the heel height worn, duration of wear (in years) and duration worn/day.

Conclusion: There was a positive correlation between duration of wear and height of footwear with regards to both heel and back pain. However, a definitive cause and effect could not be established because of smaller sample size.

Key words: Back pain, Heel pain, Shoes, Statistical analysis, Women

INTRODUCTION

Walking is the most common form of human locomotion from a motor control perspective, human bipedalism makes the task of walking extremely complex. One condition known to compound the difficulty of walking is the use of heeled shoes, which alters the natural position of the foot-ankle complex.[1] This thereby produces a chain of reaction effects that travels up to the lumbar vertebrae. High-heeled footwear is defined as the footwear having a heel that is higher than the toe. Throughout the history, this footwear is considered as a symbol of sexuality, class and gender. When the foot slants forward, a much greater weight is transferred to the ball of the foot and toes, which increases the likelihood of damage to the underlying soft tissues that supports the foot. When the wearer tips the foot forward, this in turn puts pressure on the lower back and hence causes back pain. This particular study on post-adolescent volunteers was aimed to study the correlation between heeled footwear and heel and back pain.

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MATERIALS AND METHODS

The present study was conducted on 100 female patients who attended orthopedic outpatient department at institution during the period from July 2014 to December

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2014. Patients were drafted into the study based on inclusion criteria which included:

a. Age >15 years and <55 years
b. Without any foot and spine deformities. Patients were explained about the study and only those who volunteered and gave their consent were included in this study. The procedures followed were in accordance with the ethical standards.

The evaluation was based on questionnaire which was given to all the participating volunteers and heel height was measured with the help of inch tape as illustrated in Figures 1-3. Appropriate information collected in the questionnaire was entered in data collecting sheet for the purpose of statistical analysis.

Patients were categorized based on their age group (18-25, 25-45, 45-55), occupation (student, staff, housewife), heel height (normal [<2.5 cm], low heel [2.5-5 cm] and high heel [>5 cm]), duration of wear in years (0-5 and 5-10 years) and in hours/day (0-5 and 5-10), type of sole (leather, wooden, rubber, plastic). The data collected were statistically analyzed by Chi-square test.

Observation

A total of 100 female patients were included in the study after obtaining their informed consent. There were 63 students, 28 staff, 9 housewives who participated as volunteers. There were 12 people wearing heels with height 2.5-5 cm, 4 people wearing heels with height >5 cm and 74 people wearing heels with height 0-2.5 cm. In our study, 67 people were using soft sole type and 33 people were wearing hard sole type. There were 36 people wearing heeled footwear for more than 5 years, and 54 people were using heeled footwear for 0-5 years. 15 people were wearing heeled footwear for 0-5 h/day and 85 people were wearing heeled footwear for more than 5 h a day. Regardless of heel height worn, the duration of footwear had a significant influence on heel and back pain (Table1) and similarly prolonged wear in a day had a significant influence on heel pain (Table 2).

Figure 1: Heel height being measured

Figure 2: Method of measuring heel height using measuring tape

Figure 3: Volunteers who participated in the study

DISCUSSION

Heeled footwear has been in use by women for centuries but not all individuals wearing heels suffer from clinical problems. In ancient Egypt, wearing shoes may have served to set apart lower classes from the nobility as normal people walked around bare foot while the rich wore flat leather shoes. Moreover in ancient times, height would vary so that the higher the soles, higher the social status.

Research suggests that long-term heel use can both "compromise muscle efficiency and increase the risk of injuries." Heeled shoes slant the foot forward and down while bending the toes up, more the feet is forced into this position, more it may cause the gastrocnemius muscle to shorten.

Table 1: Relationship between heel height with back and heel pain (duration of wear in years)

Heel height	Heel pain			Back pain		
	0-5 years	>5 years	Significance	0-5 years	>5 years	Significance
0-2.5 cm (74[n])	14[n]	28[n]	0.017*	32[n]	-	0.016*
2.5-5 cm (12[n])	3[n]	6[n]		3[n]	Nil	
>5 cm (4[n])	1[n]	1[n]		1[n]	1[n]	

[n]Number of patients, *As analyzed by Chi-square test

Table 2: Relationship between heel height with back and heel pain (duration of wear in hours)

Heel height	Heel pain			Back pain		
	0-5 h	>5 h	Significance	0-5 h	>5 h	Significance
0-2.5 cm	6	36	0.053*	4	28	0.456
2.5-5 cm	3	6		3	-	
>5 cm	-	2		1	1	

*As analyzed by Chi-square test

When walking in high heeled shoes, a significant reduction in ankle plantar flexor muscle movement occurs, whereas increased work is performed by the hip flexor muscle during transition from stance to swing phase. Reduced effectiveness of ankle plantar flexors during late stance results in a compensatory enhanced hip flexor pull off. Large muscle movements and increased work at hip and knee occur while wearing high heels.[2]

Wearing high heels is thought to increase an individual's likelihood of experiencing a lateral Ankle sprain. The flexed and inverted posture of the plantar while wearing high heels may increase an individual's risk of experiencing a lateral ankle sprain.[3]

Foster *et al.*,[3] found signs of increase in ankle sprains in patients wearing high heels for a prolonged duration. Esenyel *et al.*,[2] described changes in the biomechanics of walking like increase in plantar flexion in people using high heels. In the particular study, we werenot able to assess the changes in biomechanics of foot while wearing high heels as it is a purely observational study.

There is also a definitive change in subtalar joint axis while walking on a high heeled shoe in comparison to a normal shoe, hence wearing of high heel may cause foot and heel pain.[4]

High heeled shoes cause an increase in the lordotic curve of the lumbar spine.[5] Increased ankle plantar flexion causes a kinetic chain of compensation up the lower extremity that ends with hypertonic psoas muscle, producing a lumbar hyperlordosis. A hyperlordotic lumbar spine in turn will lead to back pain.

Brent *et al.*,[9] found alteration in biomechanics of the lumbar spine. In prolonged high heels wear, chain of events around the ankle were observed, like increased ankle plantar flexion which in turn led to an increase in a lordotic curve.[6]

Eisenhardt *et al.*,[5] measured pressure distribution under foot for bare feet versus heel height and found increase in distribution related to heel height. Opila-Correia *et al.*,[7] studied the kinematics of high heeled walking and found that high heeled walking was associated with increased knee flexion in the stance phase. Kerrigan *et al.*,[6] used biomechanical gait analysis and inverse dynamics to evaluate joint loadings during high heel walking and found that even moderate high heels would contribute to osteoarthritis of the knee.[8]

Electromyography analysis of the lower limb muscles in high heel users and regular footwear users showed significantly increased leg muscle activity.[9]

Based on the observations from our study done on 100 volunteers wearing heels who came to the orthopedic outpatient department for other problems, prolonged duration of wear in years/hours of wear per day resulted in heel pain that significantly affected their daily activities. Furthermore from this study, it was observed that prolonged wear of heels in due course, also resulted in back pain which again was found to be directly proportional to duration of wear in years.[10]

Even though we have derived certain conclusive results from the study, it does have few pitfalls, for instance its an observational study and results obtained were purely based on statistical analysis of the questionnaire reports. Most of the studies done on heeled footwear considered heel height more than 9 cm as high heel, whereas in our study low heel is considered <2.5 cm while heels between 2.5 and 5 cm are considered moderate and more than which is considered as high heels. Moreover, we couldnot have a definite discrimination of the type of sole worn and no changes in the final outcome with respect to the sole type worn.[11,12]

The present study did prove it right that prolonged heels wear resulted in heel pain and back pain, but concrete justification couldn't be provided as the study was done on a small group of 100 volunteers.

CONCLUSION

This study was done with an intention to break the myth or confirm the reality that high heels footwear causes heel pain and back pain. We did succeed in obtaining a stastically significant correlation between the duration of heels wear in both hours/day and a number of year worn with heel and back pain. The pitfall of this study being the minimal sample size, and it was done as an observational study based on a questionnaire evaluation.

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Original Article

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Approach to the Diagnosis of Pulmonary Tuberculosis by Private Practitioner in Jabalpur City of Madhya Pradesh, India

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Abstract

Introduction: In India, the majority of patients with respiratory symptoms initially consult to private doctors. Few studies have been performed on the role of private practitioners (PPs) in pulmonary tuberculosis (PTB) control. The present study was performed to assess the knowledge and approach to the diagnosis of PTB by PPs according to Revised National TB Control Programme and World Health Organization standard guidelines.

Aims and Objectives: Find out the approach strategy to the diagnosis of PTB by PPs in Jabalpur City of Madhya Pradesh, India.

Materials and Methods: The present study become a cross-sectional study and was conducted from January 2013 to December 2014 in an urban area of Jabalpur city of Madhya Pradesh, India. The study population included all modern medicine general practitioners (GPs) and specialists; those were practicing internal medicine including chest physicians. About 216 practitioners were participating among them 43 were considered non-responders after three visits at their practice place. So that, total numbers of practitioners interviewed were 173. All practitioners were interviewed by predesigned, semi-structured, and close-ended questionnaire during field visits.

Result: In present study, out of total participants (n = 173), (n = 148, 85.4%) were male and (n = 25, 14.6%) were female. The majority (n = 128, 74.0%,) of GPs and chest physicians opted for X-ray chest examination as the investigation of choice to diagnose PTB. About (n = 42, 24.3%), of GPs and chest physicians were used sputum examination as an investigation of choice to diagnose PTB.

Conclusion: Relying only on chest X-ray to diagnose PTB may lead to misdiagnosis, overmedication, unnecessary utilization of resources and adding extra cost to the patient. There is need to improve the awareness among PPs regarding the importance of Sputum smear examination to diagnose PTB.

Key words: Private practitioners, Pulmonary tuberculosis, Sputum, X-ray

INTRODUCTION

The Revised National Tuberculosis Control Programme (RNTCP) with the support from the World Health Organization (WHO) and STOP tuberculosis (TB) partnership, initiated the RNTCP TB Xpert Project, which adopt private practice monitoring models to provide diagnosis of TB from the private sector.[1]

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There are various standards relate to diagnosis of pulmonary TB (PTB) that should be followed by all the people treating TB patients including both practicing in the public and the private sector.[2]

There is a tendency for emphasis more on chest X-ray by general practitioners (GPs) with little use of sputum smears for diagnoses and/or follow-up of TB patients. The first step in TB control program is early detection of sputum positive cases; this should be an intensive, on-going program for the purpose of TB diagnosis and control. According to the WHO, a confirmed TB case is one from whom a biological specimen is positive by smear microscopy or culture.[3]

Unfortunately, various studies have been concluded that most of the private practitioners (PPs), never considered

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Sputum examination as necessary investigation to diagnose PTB according to standard RNTCP and WHO guidelines.

Thus, the present study aims to study the PTB diagnostic practice among the urban PPs like Jabalpur city of Madhya Pradesh, India.

MATERIALS AND METHODS

The present study become a cross-sectional study and was conducted from January 2013 to December 2014 within a period of about 2 years in an urban area of Jabalpur city of Madhya Pradesh, India. There are more than 500 doctors are practicing across the city. The total population of Jabalpur is approximately 25 lacs. The present study included 216 PPs; among them 43 were considered nonresponders after three visits at their practice places. So that, the total number of practitioners interviewed were 173. In our study pretested, semi-structured and close-ended questionnaire were used to collect the data.

Inclusion Criteria

All GPs, specialist, those were practicing internal medicine (MD) and chest physicians; with an allopathic degree from Jabalpur city.

Exclusion Criteria

Physicians, who do not have an allopathic degree, e.g., BHMS, BAMS and Unani (Hakeem, Vaidya, etc.) were excluded from the study.

Data Collection Methodology

Selection of study participants

The list of all PPs addresses and contact details were obtained from Indian Medical Association Jabalpur branch and authorized Doctor's directory of Jabalpur city and through personal contacts.

Interviews

Initially, the investigator has visited the practice place of the participants and written informed consent was obtained. A pretested questionnaires related to the study was given to each participant. Interview was conducted at the clinic of the practitioners for about 30 min. The questionnaires included basic demographic details and questions about PTB diagnostic practices. At least three clinics visits were undertaken before considering the doctor as a non-respondent.

Statistical Analysis

The data have been collected on excel sheet and results were analyzed. The results obtained were depicted in the form of tables and graphs that are self-explanatory.

RESULTS

In our study, total numbers of participants were 173. Out of them, majority of practitioners were males (n = 148, 85.5%), while only (n = 25, 14.6%) were females. Most were in the age group of 40-59 years (n = 110, 63.6%). In our study, majority (n = 133, 76.9%) of practitioners were doing practice at their private clinics whereas (n = 40, 23.1%) were doing Institutional practice. In our study (n = 26, 15%) of practitioners had been practicing for <10 years; however, about (n = 51, 29.5%) participants had more than 30 years of practice experience. Our study has shown that (n=90, 52%) of participants were examined 0-10 PTB patients per month. In our study, the majority (n = 128, 74.0%) of GPs and chest physicians opted for chest X-ray examination as the first investigation of choice to diagnose PTB and only (n = 02, 1.2%) opted sputum smear examination (Table 1 and Graph 1).

DISCUSSION

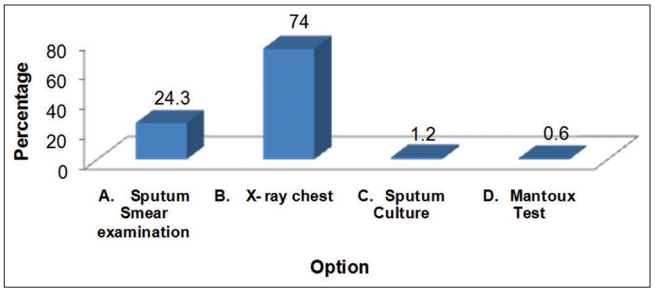
From present study, we were observed that the majority of the practitioners (74.0%) were using chest X-ray as the investigation of choice to diagnose PTB case.

Greaves *et al.*,[4] in their study observed that 80% of practitioners were using sputum microscopy as a first line test, but a variety of other tests were also employing including Mantoux test, chest X-ray, and a range of blood tests.

In a study by Khan *et al.*,[5] 96% of practitioners preferred chest X-ray and 48% sputum microscopy.

Table 1: Investigation of choice used by participants to diagnose pulmonary tuberculosis

Option	Participants	Percentage
Sputum smear examination	42	24.3
Chest X-ray	128	74.0
Sputum culture	02	1.2
Mantoux test	01	0.6



Graph 1: Investigation of choice used by participants to diagnose pulmonary tuberculosis

In a study by Okeke and Aguwa[6] most practitioners (91.2%) based their diagnosis of TB on sputum acid-fast *bacilli*.

The study conducted by Shehzadi *et al.*,[7] and Cirit *et al.*[8] were observed that bacteriology become the preferred method of diagnosis of PTB.

However, in studies from India by Prasad *et al.*,[9] Baxi and Shah[10] almost all doctors (99.8%) used Chest X-ray as an investigation of choice for diagnosis of PTB.

In a study by Pattanshetty *et al.*,[11] in Southern India observed that majority of practitioners 67.4% opted for sputum examination as the investigation of choice to diagnose PTB whereas, 26.1% had chosen sputum and chest X-ray both as a modality for diagnosis.

In a study conducted by Hong *et al.*,[12] over 50% of practitioners did not consider sputum examination essential in case finding or diagnosis of PTB.

Study done in the Philippines by Porter and Rubio[13] have observed that TB diagnosis mainly based on Chest X-ray findings (87.9%) by most of the PPs.

A study by Fidelis *et al.*,[14] for case finding and diagnosis of PTB have found that more than half (55%) of PPs were answered chest X-ray and sputum examination both; from which 30% used Chest X-ray routinely and sputum examination when considered necessary.

After discussion of other studies, we found that there are numbers of limitations of our study. As with any other participant reported survey, it is possible to have social desirability bias because PPs may answer with a response that they think as correct, rather than they are doing in their actual practice.

However, these results still show a distinct difference from the WHO and RNTCP standard recommendation to approach in the diagnosis of PTB by PPs.

CONCLUSION

Standard Guidelines are suggestive of sputum microscopy should be the first investigation for diagnosis of PTB, but our observations have been shown that most of the PPs were not following RNTCP and WHO standard guidelines, and they were using a chest X-ray. In that view, there is need to not only improve the awareness among PPs regarding the importance of sputum smear examination to diagnose PTB but also the necessity of RNTCP training for all.

Regarding the recommendations derived from the conclusions of the study, it is clear that a strong emphasis should be placed on the continuing medical education of GPs in the form of workshops and refresher courses, and through forming Public Private Partnership Scheme. Similarly, there should also be monitoring and evaluation of the standard of care in the various general practices.

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Original Article

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Effect of Single-Dose Antibiotic Prophylaxis versus Conventional Antibiotic Therapy in Surgery: A Randomized Controlled Trial in a Public Teaching Hospital

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Abstract

Introduction: Antibiotic uses in surgical procedures are varied depending on the nature of surgical procedures, environmental hygiene, and availability of drugs, especially in public hospitals. Various studies postulate prophylactic antibiotic use is cost effective than post-operative use of antibiotics.

Materials and Methods: A randomized controlled trial was done in our surgical unit in Kanyakumari Government Medical College, and the results were compared with the control group from the other surgical unit where conventional antibiotic are used for 7-10 days. All patients in study group undergoing surgeries were given 1 g cefotaxime after test dose 60 min prior to surgery. In the control group, the patients were given 3 days intravenous injection ciprofloxacin 200 mg intravenous (IV) twice a day, injection metronidazole 500 mg thrice a day, and injection amikacin 500 mg twice a day and the next 4 days the same antibiotics were given in oral route. Total 60 patients are randomized to 30 each group. The outcome of the surgery in term of duration of surgery, Surgical Site Infection, Cost and Antibiotic side effects were compared in both groups.

Results: It is observed both the duration of hospitals stay cost and side effects are significantly increased for the control group patient than the study group. Antibiotic side effects are ($P < 0.05$) for control group and cost ($P < 0.001$) were high for control group. The infection rate is similar in both groups. Grade 2 infection in 2 cases out of 30 in each group and there is no significant differences.

Conclusion: Prophylactic single-dose antibiotic is more useful and cost-effective in our public hospitals which can reduce the expenditure for drugs in country like India.

Key words: Antibiotics, Antibiotic resistance, Conventional therapy, Cost effective, Prophylaxis, Resistant bacteria

INTRODUCTION

Antimicrobial agents were considered as magic bullets and effective tools to combat infections in various therapeutic settings. However, the non-judicious usage of these antibiotics has become a subject of controversy. Rational antibiotic use is promulgated with much vigor as the resultant effect of injudicious antibiotic usage had propelled the emergence of antibiotic resistance and spiraled the cost escalation in therapeutic care.[1]

Antibiotic resistance has become a global menace, and WHO in 2012 had given a clear call to reduce the antibiotic use and prevent resistance to antibiotics.[2]

Antibiotic prophylaxis is a therapeutic method in which antimicrobial agents are used prophylactically to prevent the infectious complications in a therapeutic procedure.

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In conventional antibiotic use, antimicrobials are used for a predetermined period after therapeutic procedure to combat the infection.[3]

Various techniques of antibiotic prophylaxis, the quantities and nature of drug use, timing of the use of the drug were studied by various cross-sectional studies and based on the data the standard protocol of antibiotic prophylaxis for each procedure were randomized and published.[4]

In this era of antibiotics, the cornerstones of infection control, such as meticulous surgical skill, respectful tissues handling, inbuilt environmental sanitation, adequate preoperative preparation, congenial theater environment, and adequate wound care, are given less priority.[5]

As per various studies cited and Cochrane data reviewed the conventional use of antibiotic for much longer period are not justified.

Most often in public hospitals where the environmental hygiene is not adequately maintained and over load of surgical patients with the fear of development of surgical site infections even for clean and clean-contaminated surgeries antibiotics are given for 7-10 days. The traditional approach for this multi dose usage often leads to huge expenditure to the hospital and enhance emerging of resistance to the particular drug and the group to which it belong.

Hence, this study is intended to study the effect of single-dose antibiotic prophylaxis given 60 min prior to surgery with the standard chosen antibiotic versus the conventional use of same antibiotics for 7 days or until the patient is discharged from the hospital.

MATERIALS AND METHODS

This study was conducted as a randomized case-control prospective study in the Department of Surgery in Kanyakumari Government Medical College Hospital from 2014 July to 2015 July. Totally 60 patients admitted for clean surgery in our hospital without any co-morbid conditions were included in this study.

The patients were randomized into study group in one surgical unit getting admission on Wednesday and patient getting admitted to Thursday unit is included as a control.

All the surgeries were carried out in the same theater environment, and same preoperative safety protocol, and post-operative care is followed for all patients.

The Use of Antibiotics are Predetermined as Follows

Study group

One dose of 1 g injection cefotoxim IV after test dose 60 min prior to surgery and no more antibiotics are prescribed.

Control Group

No pre-operative antibiotic given. In the post-operative ward for the first 3 days IV antibiotics are given as follows:

- Injection ciprofloxacin 200 mg IV bd
- Injection metronidazole 500 mg IV tds
- Injection amikacin 500 mg IV bd.

Next 4 days:

- Tablet ciprofloxacin 200 mg oral bd
- Tablet metronidazole 400 mg oral tds.

Ethical Aspect

The study proposed was approved by the Ethical Committee of our institution. All participants were provided and obtained informed consent after explaining all the features of studies.

Inclusion Criteria for the Surgical Patients

Patients with the age group 20-60 both male and female with no co-morbid conditions and posted for following surgeries are included in the study.

1. Inguinal hernia all type undergoing lichen stein mesh repair
2. Hydrocoel for eversion of sac
3. Varicose vein for trendlenberg operation
4. Umblical hernia for mesh repair
5. Epigastric hernia for mesh repair
6. Benign thyroid condition for hemi/subtotal thyroidectomy.

Exclusion Criteria

- History of hypersensitivity to cephalosporin group of antibiotics
- Patient with co-morbid renal, cardiac, hepatic damages
- Patient on steroid or having immune deficiency
- Non-willing patients
- Patients on long-term medication for diabetes, hypertension, or psychiatry problems.

Demographic Variable

The age, sex, height, weight, and socio-economic status were studied.

Variables Measured

- Duration of surgery
- Development of infection based on Southampton grade
- Cost of antibiotics
- Complications due to the side effects of antibiotics.

Pre-operative Preparation and Care

All the patients posted for these elective surgeries were admitted on the day prior to surgery. All necessary investigation are done and anesthetic fitness obtained. The operative site was cleaned/shaved with aseptic precaution. All patients were asked to take body bath with soap on the day of surgery and the operative site covered with a sterile dressing.

Aseptic Precautions in the Operation Theater

Theater asepsis is maintained, and checklists were verified. All the instruments were counter checked for sterility from CSSD Department. Standard surgical scrub for 5-10 min mandatorily followed by the surgical team.

Operation Techniques

After anesthesia, the operative site is prepared with povidine iodine and spirit. The principles of surgery, especially minimal tissue handling, adequate hemostasis, less use of cautery, appropriate use of drains were followed. Wound closed without tension, and a sterile dressing applied.

Post-operative Care

The patient were kept in the post-operative ward for 3 days and shifted to general ward after 3 days. Temperature and vitals are monitored periodically, and the charts are maintained. Wound inspection was done on 3rd, 5th, and 7th day. Dedicated staff followed up with the drugs to be administered and ensured the antibiotics are given at appropriate time as per the protocol.

OBSERVATION AND RESULTS

Total 60 patients undergoing surgical procedures were taken into two groups. Patients in the control group undergoing surgical procedures were given, 7 days of antibiotics and discharged on the 8th day after removal of suture materials. 30 patients were grouped into study group, who got only one dose of prophylactic antibiotic 1 h before surgery. The Demographic profile of all patients in both the group were studied and tabulated in Table 1 and Figure 1.

Demographic Profile

The patients in the both group have undergone following surgeries and number of patients for each surgery in each group were tabulated in Table 2 and Figure 2.

The mean weight, hemoglobin level, type of anesthesia, and duration of surgery for each group of patients in different surgeries were measured and tabulated in Table 3.

Antibiotic Profile

Study group

1. Injection cefotoxim 1 g IV 1 h prior to surgery
2. 3rd day dressing changed and checked for infection
3. Daily dressing with saline
4. Suture removed on the 5-6th day.

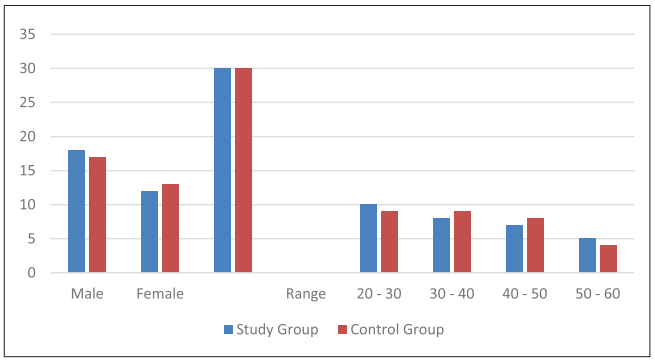

Figure 1: Demographic profile

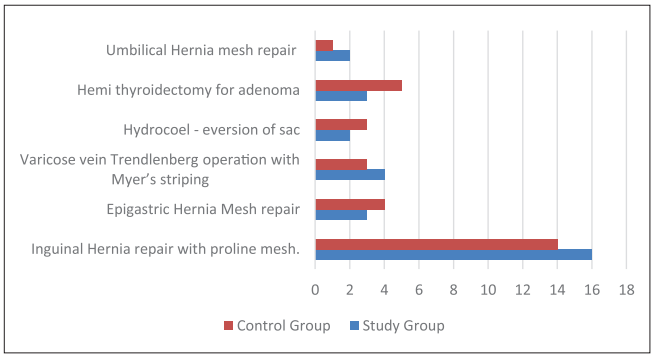

Figure 2: Nature of surgery in each group

Table 1: Demographic profile of the study and control group

Average cost	Study group	Control group
Sex		
Male	18	17
Female	12	13
Total	30	30
Mean age		
Range		
20-30	10	9
30-40	8	9
40-50	7	8
50-60	5	4

Table 2: Nature of surgery in each group

Nature of surgery	Study group	Control group	Total
Inguinal hernia repair with proline mesh	16	14	30
Epigastric hernia mesh repair	3	4	7
Varicose vein trendlenberg operation with Myer's striping	4	3	7
Hydrocoel - eversion of sac	2	3	5
Hemithyroidectomy for adenoma	3	5	8
Umbilical hernia mesh repair	2	1	3
Total	30	30	60

Table 3: Mean Hb status, weight, duration of surgery and type of anesthesia

Type of surgery	Study group				Control group			
	Weight	Hb	Type of anesthesia	Duration of surgery (min)	Weight	Hb	Type of anesthesia	Duration of surgery (min)
Inguinal hernia	52	9.6	Spinal	45	53	9.8	Spinal	48
Epigastric hernia	70	9.8	Spinal	45	69	9.6	Spinal	56
Varicose vein	54	9.4	Spinal	50	52	9.3	Spinal	53
Hydrocele	53	9.6	Spinal	30	51	9.5	Spinal	35
Hemi thyroidectomy	48	9	GA	60	47	9.1	GA	45
Umbilical hernia	51	9.4	Spinal	45	52	9.3	Spinal	50

Hb: Hemoglobin, GA: General anesthesia

Control Group

1. First 3 days
   - Injection metronidazole 500 mg IV tds
   - Injection ciprofloxacin 200 mg IV bd
   - Injection amikacin 500mg IV bd
2. Next 4 days
   - Tablet ciprofloxacin 500 mg oral bd
   - Tablet metronidazole 400 mg oral tds
3. 3rd day dressing changed and checked for infection
4. Daily dressing with betadine solution
5. Suture removal on the 6th and 7th day.

Infection Grading in the Ward

Based on the Southampton scoring system on the 3rd, 5th, and 7th post-operative period the wounds were inspected and the infection grades are noted.

Southampton Scoring System

Grade:
0 = Normal healing
1 = Bruising and mild erythema
2 = Erythema and signs of inflammation
3 = Clear (or) serous discharge
4 = Pus formation
5 = Deep, severe wound infection.

Out of the 60 patients' only 4 patients, 2 in each group shown infection in the post-operative period. 2 had grade 1 infection, and another 2 had grade 3 infection. No change in the protocol done. On dressing and saline wash infections controlled and all patient were discharged with the good general condition. No statistically significant difference with infection prolife noted in both the group. The results are tabulated in Table 4.

Cost Estimation

The cost involved for the each patient for the antibiotics and syringe usage are calculated for each patient in average. The study group antibiotic cost was only 30 rupees while for each patient in the control group it was more than 890 rupees. On statistical analysis, it shows gross significance with *P* factor < 0.001. The cost for each patient in average is tabulated in Table 5.

Table 4: Grade of post-operative infections

Grade of infection	Study group			Control group		
	3rd day	5th day	7th day	3rd day	5th day	7th day
Grade I	-	1	-	-	1	-
Grade II	-	-	-	-	-	-
Grade III	-	1	-	-	1	-
Grade IV	-	-	-	-	-	-
Grade V	-	-	-	-		-

Table 5: Average cost of antibiotics

Average cost	Study group	Control group	*P* factor
Cost of antibiotics	Rs. 30/patient	Rs. 890/patient	0.001

Side Effects of Antibiotic Treatment

All patients were observed for the known side effects of the drugs used and also watched for adverse drug reactions. No patients had adverse drug reactions from both the groups.

None developed antibiotic side effects in the study group. In control group, four patients had severe metallic taste and one patient had urticarial rash following the antibiotic use.

DISCUSSIONS

This randomized control study to assess the effectiveness of one dose of prophylactic antibiotic versus the traditional use of 7 days antibiotics has shown no significant difference in the wound infection rate in both the groups. However, there is a significant increase in the cost and side effects of antibiotics in the control group using conventional 7 days antibiotics.

The use of prophylactic antibiotic in all surgical cases are advocated ever since, the concept of use of antibiotic pre-operatively to curtain and prevent wound infection was postulated by Bernard and Cole in 1964.[6]

The overall experience from across the world has categorically recommended using the specific antibiotics in the pre-operative period than traditional use of 5-7 days of antibiotics in the post-operative period.

With much advancements in the asepsis of the environment and hygiene of the theaters, it was questioned in many surgical settings on the need of antibiotic at all for clean and clean-contaminated surgical cases. However, in high turnover hospitals in public setting, even while all the sterile precautions are adhered too, the surgical procedures can imbibe bacteria or other microbial agents in the blood and lead to bacteremia the use of long-acting antibiotic to cover the perioperative period is recommended.[7]

In 2001, Chambers in their study recommended that first generation cephalosporin antibiotic the cefazolins are drugs of choice for the use of prophylactic antibiotics for the general surgical prophylaxis than the second or third generationcephalosporin.[8]

Naz in a comparative study between a single-dose cephradine as the prophylactic antibiotics versus conventional dose of antibiotics in major gynecological procedures have stated prophylactic antibiotic use is adequate provided standard principles of operative surgery are adhered.[9]

Wideman and Matthijssen in his study conducted on the use of cefazolin versus cefotaxime as the prophylactic antibiotic in 118 hysterectomy patients in 1982 stated cefotaxime and cefazolin are equally beneficial on all aspect, and use depend on the cost and availability.[10]

Many studies have been conducted on the choice of antibiotic and timing of use of antibiotics. Most of the studies have recommended the first dose to be given 30-60 min prior to surgery, and long-acting antibiotic must be selected.[11]

Fernandez Arjona *et al.* had conducted a study to find out the economic advantages following use of prophylactic antibiotic rather than traditional 7 days antibiotics, using 5260 patients in a medical Centre in Southern Taiwan and stated that use of prophylactic antibiotic alone for the surgical patients had resulted in gain of 1.5 million dollars for the public.[12]

Our study also proves, there is a significant advantage of economic gain when only prophylactic antibiotic is used.

Antibiotic are magic bullets but inadvertent and over use can cause potential side effects and also leads to the development of drug resistance bacteria. In our study, it is noted a significant number of the patient had developed side effects of antibiotic during this period.

More than the antibiotics clean surgical environment, hand washing, adequate preparation of patients and following universal precaution will improve the wound healing and prevent the infection in the patient.

CONCLUSION

Our study concludes that even in public institutions where the turnover of the patients are the high judicious use of prophylactic antibiotic alone can prevent any wound infections which will lead to potential economic benefits and prevent the development of resistant strains of bacteria.

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Original Article

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Comparative Study on Efficacy of Autologous Platelet Gel versus Topical Phenytoin in Chronic Wounds: A Prospective, Randomized Controlled Study

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Abstract

Introduction: Platelets are commonly known to release certain factors from alpha (α) granules which include platelet-derived growth factor and epidermal growth factor, which act locally on the wound and hasten the healing process. The most common side effect of phenytoin treatment for epilepsy is gingival hyperplasia.

Aims: The objective of this study was to assess the efficacy of Autologous Platelet gel compared to topical phenytoin in improving the healing process and to prove it as a relatively low cost and easy to use the option in the management of chronic wounds.

Materials and Methodology: In this experimental study, the data from 30 patients with chronic ulcers were collected, 15 patients underwent topical phenytoin dressing, and remaining 15 patients underwent autologous platelet gel. Variables like the rate of granulation tissue formation as percentage of ulcer area covered, percentage of graft take up, and duration of hospital stay were compared.

Results: Mean reduction in the area of ulcer, 237.67 mm2 for the platelet dressing was more than that of phenytoin dressing, 17.04 mm2 after the initiation of treatment. The percentage reduction in platelet dressing was 46.95% ± 15.16% and 2.28% ± 2.54% in phenytoin dressing, which was statistically significant. The maximum number of days in which granulation tissue was seen in platelet dressing is 1-10 days, i.e., 80% and in phenytoin dressing the maximum number of days in which granulation tissue was seen is 11-20 days, i.e., 53.0%.

Conclusions: Autologous platelet gel helps in faster healing with better graft take up and reduces hospital stay.

Key words: Chronic wounds, Dressing, Granulation tissue, Healing, Phenytoin, Platelet gel

INTRODUCTION

Platelet extract has shown to enhance and accelerate both soft tissue and hard tissue healing. Its effectiveness is based on its high level of growth factors such as platelet-derived growth factor (PDGF), transforming growth factor-β, epidermal growth factor (EGF), vascular EGF, and insulin-like growth factor.[1]

A common side effect of phenytoin is the development of fibrous overgrowth of gingiva. This apparent stimulatory effect of phenytoin on connective tissue suggested an exciting possibility for its use in wound healing. It has been reported that phenytoin has contributed to the removal of various Gram-positive and Gram-negative organisms from wounds. Local pain relief has been observed with topical phenytoin therapy, which can be explained by its membrane stabilizing action and by reducing the inflammatory response. Facilitation of nerve regeneration has also been reported with phenytoin.[2]

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MATERIALS AND METHODOLOGY

This is a prospective, randomized controlled study, to test the efficacy of autologous platelet gel versus topical phenytoin in epithelialization and wound reduction in chronic wounds. The study was conducted in the Department of Surgery, JSS hospital for a period of 6 months from July 2014 to December 2014.

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30 patients were studied, 15 cases were randomly chosen for study with autologous platelet gel and 15 cases received topical phenytoin as dressing for the chronic wound.

- Study type:
  - Prospective, observational, randomized study.

Inclusion Criteria

- Age group: 18-80 years
- Ulcer ≥ 8 weeks
- Hemoglobin > 10 g%
- Fasting blood sugar ≤ 110 mg% and Post-prandial blood sugar ≤ 140 mg% if diabetic.

Exclusion Criteria

- Ulcers with evidence of malignancy
- Active infection with pus discharge, slough
- Evidence of gangrene in the ulcer or on any other part of limb
- Patient is currently receiving or has received radiation or chemotherapy within the last 3 months
- Patient has known or suspected osteomyelitis
- Patient with active cancer, decompensated liver disease, or on renal dialysis
- Patients on steroids for another illness
- Patients on oral phenytoin
- Patients hypersensitive to phenytoin.

Preparation of Platelet Gel

- 12 ml of blood was drawn intravenously from the antecubital region
- Blood centrifuged at 1000 rpm for 10 min
- The supernatant formed is platelet poor plasma which is discarded
- Remaining PRP is collected in another vacutainer and again centrifuged at 1000 rpm for 10 min. The upper half is discarded, and the lower half yields concentrated platelet rich plasma
- 2 ml of PRP which is thoroughly mixed with 0.08 ml of 10% calcium gluconate.

Topical Phenytoin

A single 100 mg phenytoin sodium capsule was opened and placed in 5 ml of sterile normal saline to form a suspension. Sterile gauze was soaked in the suspension and placed over the wound at 20 mg/cm^2 total body surface area.

RESULTS

In this study, 90% of the patients were males as compared to females who were 10% of the total cases as shown in Table 1 and Graphs 1 and 2.

In this study, 50% of the wounds were of non-specific traumatic etiology. The next most common wounds were pressure sores at 16.6%. There is no statistical difference between platelet dressing and Phenytoin dressing with regard to the etiology of the wounds ($P = 0.797$) as shown in Table 2.

The mean duration of the wound in platelet dressing was 103.73 ± 130.75 weeks and 52 ± 98.2 weeks in the phenytoin dressing group. The difference of mean duration of the wound in platelet dressing and phenytoin dressing was not statistically significant ($P = 0.231$) as shown in Table 3 and Graph 3.

The mean area at the beginning of the study was 518.73 ± 383.02 mm^2 in the platelet dressing and 517.73 ± 506.91 mm^2 in the phenytoin dressing. There was no statistical difference between the two groups ($P = 0.995$) before initiation of treatment as shown in Table 4.

Mean reduction in the area of ulcer, 237.67 mm^2 for the platelet dressing was more than that of phenytoin dressing, 17.04 mm^2 after the initiation of treatment, and

Table 1: Age at presentation

Age group (in years)	No of patients	Percentage	*n*=15 (%)	
			Platelet dressing	Phenytoin dressing
<20	1	3	0 (0)	1 (7)
20-40	7	24	4 (27)	3 (20)
40-60	16	53	8 (53)	8 (53)
60-80	6	20	3 (20)	3 (20)

Table 2: Various etiologies of wounds

Etiology	Platelet dressing (%)	Phenytoin dressing (%)	Total (%)
Non-specific traumatic	8 (53.3)	7 (46.6)	15 (50)
Pressure sore	3 (20)	2 (13.3)	5 (16.6)
Diabetes	1 (6.7)	3 (20)	4 (13.3)
Snake bite	2 (13.3)	2 (13.3)	4 (13.3)
Varicose veins	1 (6.7)	1 (6.7)	2 (6.7)

Table 3: Duration of wound

Type of dressing	Duration in weeks		*P*
	Mean	SD	
Platelet dressing	103.73	130.75	0.231
Phenytoin dressing	52	98.2	

SD: Standard deviation

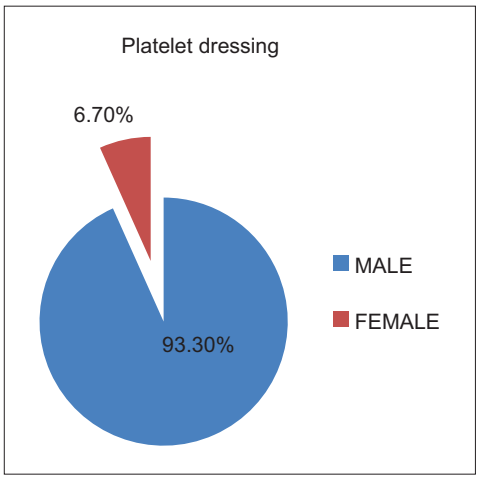
Table 4: Initial wound area in mm^2

Type of dressing	Before		*P*
	Mean	SD	
Platelet dressing	518.73	383.02	0.995
Phenytoin dressing	517.73	506.91	

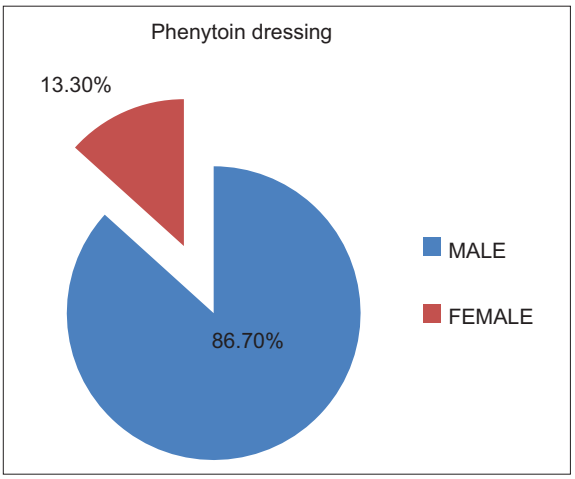
SD: Standard deviation

the difference was statistically significant ($P < 0.001$) as shown in Table 5 and Graph 4.

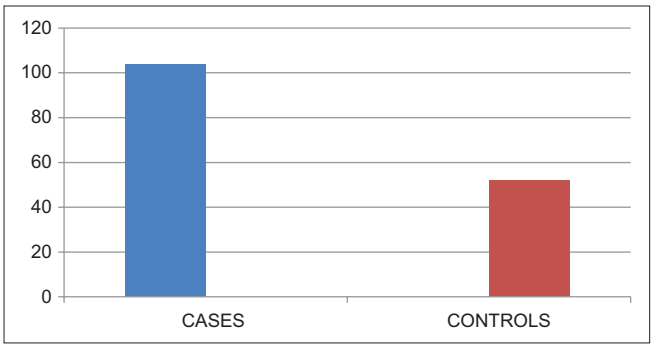
The percentage reduction in platelet dressing was 46.95% ± 15.16% and 2.28% ± 2.54% in phenytoin dressing which was statistically significant ($P = 0.000$) as shown in Table 6.



Graph 1: Platelet dressing



Graph 2: Phenytoin dressing



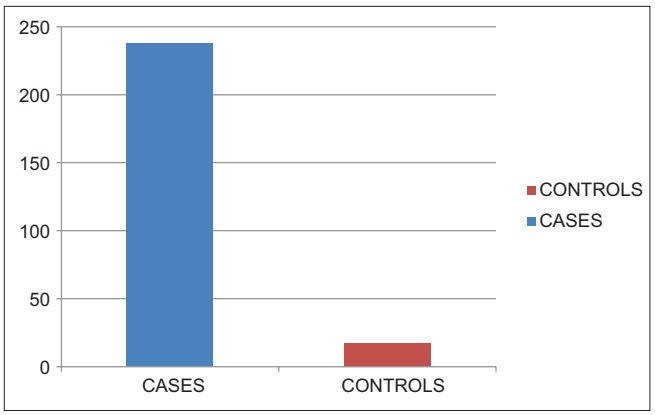
Graph 3: Mean duration of wound in cases and controls

Mean granulation is significantly less in platelet dressing with $P \leq 0.001$. The maximum number of days in which granulation tissue was seen in platelet dressing is 1-10 days, i.e., 80% and in phenytoin dressing the maximum number of days in which granulation tissue was seen is 11-20 days, i.e., 53.0% as shown in Table 7, Graph 5 and Figure 1.

DISCUSSION

Autologous platelet-rich plasma for the treatment of chronic wounds has been under development as a theory and for clinical application since 1986 when Knighton *et al.*[3] demonstrated for the first time its use in stimulating repair of non-healing human wounds.

In the Knighton *et al.* study,[3] the experimental group had a longer duration than the control group (119 weeks compared to 47 weeks), whereas in the Anitua *et al.* study,[4] the wound duration was longer in the control group (110 weeks vs. 68 weeks). The remaining studies including



Graph 4: Mean reduction in area of ulcer between cases and control

Figure 1: Rate of granulation formation at day 1 and day 4 after platelet dressing. (a) Day 1 platelet dressing, (b) Filling of wound bed and Rim of epithelialization, (c) Day 4 platelet dressing

Table 5: Reduction of mean area of ulcer of platelet dressing and phenytoin dressing after treatment

Type of dressing	Mean area reduced in mm²	SD	*P*
Platelet dressing	237.67	194.02	<0.001
Phenytoin dressing	17.07	33.30	

SD: Standard deviation

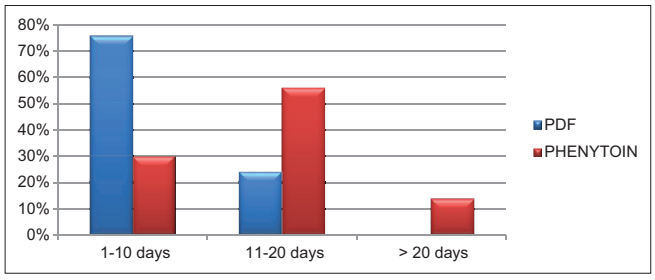
Table 6: Percentage reduction of wounds

Type of dressing	Percentage reduction		*P*
	Mean	SD	
Platelet dressing	46.95	15.16	0.000
Phenytoin dressing	2.28	2.54	

SD: Standard deviation

Table 7: Comparison of number of days in which granulation tissue appeared in both the groups

Granulation	Platelet dressing (*n*=15)		Phenytoin dressing (*n*=15)	
	No.	%	No.	%
1-10	12	80.0	4	26.0
11-20	3	20.0	8	53.0
>20	0	0.0	3	20.0



Graph 5: Rate of granulation tissue formation in days

the present study had no statistical difference of wound duration between cases and controls.

The mean size of the wounds in the present study was 51.7 cm^2 which is much higher than in the other studies being 4 times more than the next largest in the series, 13 cm^2 of the Krupski *et al.* study.[5]

In the present study, the rate of healing in the phenytoin group was 0.85 ± 1.67 cm^2/week and in the platelet group was 11.87 ± 9.71 cm^2/week ($P < 0.05$).[6]

The final area of the wounds was significantly reduced in the platelet group as compared to the phenytoin group at the end of the study.

The time taken per platelet dressing was 30-40 min. No cost was incurred by the patient as all materials required were available as hospital supply. No adverse effects were seen with platelet dressing. The growth factors present in platelets are the individual patient's natural growth factors in their biologically determined ratio. Because it is autologous, it presents no risk of immunogenic reactions or human to human disease transmissions like HIV or hepatitis B, thus making it a safe modality of treatment.

The study, in spite of its shortcomings, does indicate that topical application of autologous platelet is more effective than topical phenytoin therapy in helping a chronic ulcer to heal and that it has the potential to be a useful, safe, and cost-effective adjunct to wound healing.

CONCLUSION

With the use of autologous PDGF dressings in comparison with topical phenytoin therapy for the treatment of chronic ulcers, the following conclusions were derived.

- PDGF showed faster and better healing rates among the study group
- Area reduction was statistically significant in the study group
- There were no adverse effects or reactions seen both the group
- The overall hospital stay and post-operative complications were less in both groups.

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Original Article

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Dermatological Disorders in Pregnancy: A Cross-Sectional Study

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Abstract

Introduction: During pregnancy immunologic, metabolic, endocrine, and vascular changes occur, which make the pregnant woman susceptible to changes of the skin and appendages, both physiologic and pathologic.

Aims: We undertook a clinical study to find out the frequency and pattern of dermatological disorders in pregnant women.

Material and Methods: All consecutive pregnant women attending skin out-patient department with dermatological disorders over a period of 3-year between August 2011 and November 2013 at our tertiary care hospital are included.

Results: A total of 372 pregnant women were included in this study. Out of these, 146 (39.25%) pregnant women were primigravida and 226 (60.75%) were multigravida. Skin disorders grouped into specific dermatoses (81 cases) and other dermatoses affected by pregnancy (291 cases). In various specific dermatoses of pregnancy, atopic eruptions of pregnancy were the most common disorder (53 cases). The most common infectious dermatoses affected by pregnancy were vulvovaginal candidiasis (58 cases) and non-infectious dermatoses affected by pregnancy were acne vulgaris (14 cases).

Conclusion: This study brings focus on pregnancy-specific and non-specific dermatoses.

Key words: Pregnancy non-specific dermatoses, Pregnancy-specific dermatoses, Sexually transmitted disease in pregnancy

INTRODUCTION

Pregnancy is characterized by alteration in endocrine, metabolic, vascular, and immunity system resulting in multiple cutaneous changes, which are physiological and pathological.[1] Physiological skin changes in pregnancy include changes in pigmentation, alterations of the connective tissue, vascular system, and hormonal function.[2]

The pre-existing skin conditions may either improve or exacerbate during pregnancy due to immunological, endocrinal, metabolic, and vascular changes in pregnancy.[3] A typical examples is psoriasis, a classical Th1-associated disease, which often improves in pregnancy.[4] Diseases primarily associated with a Th2-immune response, such as lupus erythematosus and other autoimmune dermatoses,[5] which deteriorate during pregnancy and improves after delivery. Acne vulgaris often improves but can worsen during pregnancy.[6] The severity and frequency of skin infections are increased, Because of depressed cell-mediated immunity during pregnancy.[7]

Pregnancy-specific dermatoses represent a severely pruritic and inflammatory heterogeneous group of dermatoses associated exclusively with pregnancy and/or the immediate post-partum period.[8] The rarity of these diseases, variability of morphology, and a lack of unequivocal diagnostic tests as well as limited treatment options leads to confusing terminologies and have made their management difficult. Recently, a new classification of pregnancy specific dermatoses has been established, based on the results of a retrospective study on more than 500 pregnant patients.[9]

Sexually transmitted diseases (STDs) remain a major global health concern.[10] Women are the most vulnerable

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population to STDs and HIV. The florid manifestation of STDs is seen in pregnant women. The effect of pregnancy is additive to the immune suppression was seen in AIDS.[11]

This study includes pregnancy specific, non-specific dermatological disorders and STD in pregnancy.

Aims and Objectives

1. To study different specific and non-specific dermatological disorders in pregnancy
2. To study the association between dermatological disorders and trimesters of pregnancy
3. To study STD in pregnancy.

MATERIAL AND METHODS

A cross-sectional study was conducted in the outpatient Department of Dermatology and VD in Smt. SCL Hospital, Ahmedabad. All pregnant women with dermatological disorder attended between August 2011 and November 2013 are included in this study, Irrespective of the duration of pregnancy and gravidity. A total of 372 pregnant women are included in the study. Informed consent was obtained before the interview and clinical examination. Detailed history including demographic data, chief complaints related to skin, onset in relation to duration of pregnancy, past or family history of similar lesions, exacerbating factors, associated medical or skin disorders, etc. were elicited and recorded.

The complete cutaneous examination was done. If any specific dermatoses of pregnancy are present, the morphology of skin lesions, distribution and the sites involved were studied. The relevant systemic examination was carried out. If any preexisting skin disease is present, any evidence of exacerbation or remission were recorded. Appropriate investigations were done to confirm the diagnosis. Bedside this, laboratory procedures like Tzanck smear, KOH mount, Wet mount, pH and Gram's stain were carried out. To confirm the diagnosis skin biopsy were done in a few cases.

Inclusion Criteria

All pregnant women with dermatological disorders irrespective of the duration of pregnancy and gravidity.

Exclusion Criteria

Pregnant women with physiological skin changes.

RESULTS

A total of 372 pregnant women were included in our study from August 2011 to November 2013. Out of them, 146 (39.25%) were primigravidas and 226 (60.75%) were multigravidas (Tables 1-3 and Figure 1).

In this study, total patients with non-specific non-infectious disorder were 101, most of them presented in the 3rd trimester - 54 cases (53.47%), followed by in 2nd trimester - 37 cases (36.63%) and 1st trimester - 10 cases (09.90%).

In present study, Acne vulgaris (14 cases [13.86%]) was the most common non-specific non-infectious disorder, followed by chronic eczema (12 cases [11.8%]) and urticarial (10 cases [9.90%]). Rest of all other diseases accounted for < 8% each (Figure 2).

In this study, most of patients with infectious disorders were presented in 3rd trimester -100 cases (52.6%), followed by in 2nd trimester - 64 cases (33.58%) and in 1st trimester - 26 cases (13.54%).

Out of total infectious disorders (190 cases); vulvovaginal candidiasis (VVC) was the most common disorder, was presented in 58 cases (30.53%), followed by bacterial

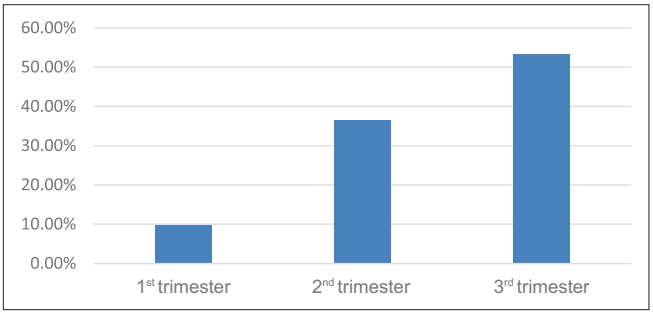

Figure 1: Analysis of patients with non-specific non-infectious disorders according to trimester

Table 1: Age group wise distribution of patients with dermatological disorders

Age group	Number of patients (%)
<20	53 (14.25)
21-30	300 (80.65)
31-40	19 (5.10)
>40	0
Total	372 (10)

Table 2: Analysis of total number patients according to trimester

Trimester	Number of patients (%)
First	37 (9.95)
Second	120 (32.26)
Third	215 (57.80)
Total	372

Table 3: Analysis of patients with pregnancy specific disorders according to trimester and gravida

Disease	1st trimester (%)	2nd trimester (%)	3rd trimester (%)	Number of primigravida (%)	Number of multigravida (%)	Total (% of disorders from total pregnancy specific disorders) (%)	% of disorders from total no of dermatological disorders in pregnancy (372 cases) (%)
Atopic eruption of pregnancy	9 (11.11)	15 (18.51)	29 (35.80)	17 (32.07)	36 (67.93)	53 (65.43)	14.25
PUPPP	0	2 (2.4)	17 (20.99)	15 (78.95)	4 (21.05)	19 (23.45)	5.11
ICP	0	1 (1.23)	4 (4.93)	3 (60)	2 (40)	5 (0.06)	1.34
PG	1 (1.23)	0	1 (1.23)	1 (50)	1 (50)	2 (2.46)	0.54
Impetigo herpetiformis	0	0	2 (2.46)	2 (100)	0	2 (2.46)	0.54
Total	10 (12.34)	18 (22.22)	53 (65.44)	32 (39.51)	49 (60.49)	81 (100)	21.77

PUPPP: Pruritic uricarial papules and plaques of pregnancy, ICP: Intrahepatic cholestasis of pregnancy, PG: Pemphigoid gestationis

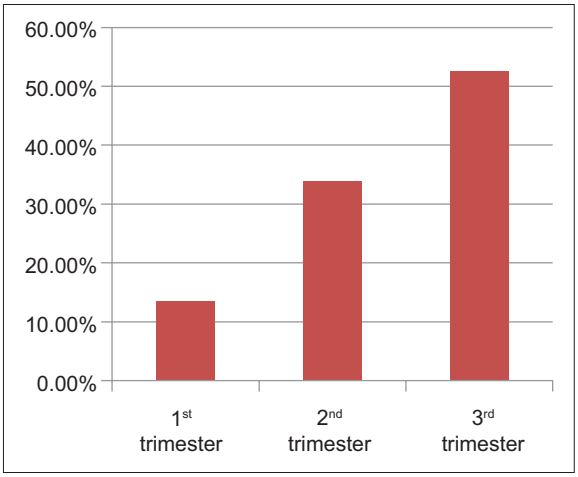

Figure 2: Analysis of patients with infectious disorders according to trimester

vaginosis (BV) in 22 cases (11.58%), tinea in 17 cases (8.95%), scabies in 13 cases (6.84%), trichomonas vaginitis in 11 cases (5.79%), candidial intertrigo in 10 cases (5.26%) and rest of all diseases in < 5% cases (Tables 4 and 5).

DISCUSSION

Common skin conditions during pregnancy generally can be separated into three categories:[12] (1) Physiological: Hormone-related, (2) preexisting (non-specific dermatological disorders) and (3) Pregnancy-specific dermatological disorders. In this literature, we found various dermatological specific and non-specific disorders associated with pregnancy.

We enrolled total 372 pregnant women with the dermatological disorder for study irrespective of the duration of pregnancy and gravidity. The most common presenting age group of women with dermatological disorders was 21-30 year. 146 patients (39.25%) were primigravidas and 226 patients (60.75%) were multigravidas.

Table 4: Patients with similar complain in previous pregnancy in pregnancy specific disorder

Disease	Number of patients (%)
Atopic eruptions	20 (76.92)
PUPPP	3 (11.54)
ICP	2 (7.69)
PG	1 (3.84)
Total	26

PUPPP: Pruritic uricarial papules and plaques of pregnancy, ICP: Intrahepatic cholestasis of pregnancy, PG: Pemphigoid gestationis

Table 5: Analysis of patients presented with STD

STD	Total	% of diseases from total no of STD (128)	% of diseases from total no of dermatological disorders (372)
VVC	58	45.31	15.59
BV	22	17.19	5.9
Trichomonas vaginitis	11	8.59	2.96
Herpes progenitalis	9	7.03	2.41
Genital wart	5	3.90	1.34
Gentital molluscum	5	3.90	1.34
Syphilis	4	3.13	1.08
HIV	14	10.94	3.76
Total (34.41%)	128		34.41

STD: Sexually transmitted diseases, VVC: Vulvovaginal candidiasis, BV: Bacterial vaginosis

Total patients with pregnancy-specific dermatological disorders were 81 cases (21.77%). Most of them presented in 3rd trimester - 53 cases (65.44%), followed by 2nd trimester - 18 cases (22.22%) and 1st trimester - 10 cases (12.34%). In pregnancy specific dermatoses most common was atopic eruptions of pregnancy in 53 cases (65.43%); followed by pruritic uricarial papules and plaques of pregnancy (PUPPP) in 19 cases (23.45%), intrahepatic cholestasis of pregnancy (ICP) in 5 cases (0.06%); and same number of pemphigoid gestationis (PG) in 2 case (2.46%) and impetigo herpatiformis 2 cases (2.46%). All of pregnancy specific dermatoses mostly found in the 3rd trimester of pregnancy. In pregnancy specific disorders, patients with similar complain in previous pregnancy were

total 26, out of them 20 (76.92%) patients with atopic eruptions of the pregnancy, followed by 3 cases (11.54%) of PUPPP, 2 cases (7.69%) of ICP, 1 case of PG (3.84%).

Total non-specific dermatological disorders were 291 cases (78.23%). Out of total patients of non-specific disorders non-infectious were 101 cases and infectious were 190 cases. Most of patients with non-infectious condition - 54 cases (53.47%) and infectious condition - 100 cases (52.6%) presented in the 3rd trimester. Acne vulgaris (14 cases [13.86%]) was the most common non-specific non-infectious disorder, followed by chronic eczema (12 cases [11.8%]) and urticarial (10 cases [9.90%]). VVC was the most common infectious disorder, presented in 58 cases (30.53%), followed by BV in 22 cases (11.58%), tinea in 17 cases (8.95%), scabies in 13 cases (6.84%), trichomonas vaginitis in 11 cases (5.79%), candidial intertrigo in 10 cases (5.26%), and others were < 10 in number.

Total 128 (34.41%) patients were presented with STD. Most of patients with VVC - 58 (45.31%), followed by 22 (17.19%) patients with BV, 11 (8.59%) patients of trichomonas vaginitis, 9 (7.03%) patients of herpes progenitalis, 5 (3.90%) patients of genital wart, 5 (3.90%) patients of genital molluscum, 4 (3.13%) patients of syphilis (venereal disease research laboratory positive) and 14 (10.94%) patients of HIV.

Total 14 patients were diagnosed as having HIV infection. Out of them 4 (28.57%) patients were presented with herpes progenitalis, 5 (35.71%) patients with VVC, 3 (21.43%) patients with BV, 1 patient (7.14%) with trichomonas vaginitis and 1 patient (7.14%) with plantar dyskeratosis.

We found 3 studies Kumari *et al*.,[13] Shivakumar and Madhavamurthy[14] and Raj *et al*.[15] having maximum similarity with our study.

In 2007, Kumari *et al*.[8] reported a study of 607 pregnant women. Skin changes grouped into physiological changes (all cases), specific dermatoses (22 cases) and other dermatoses affected by pregnancy (125 cases). In this study, total 147 patients presented with dermatological specific and non-specific disorders were included. In 1999, Shivakumar and Madhavamurthy[9] studied 170 cases of pregnant women with skin and STDs. In 1992, Raj *et al*.[10] screened 1175 pregnant women for cutaneous disorders. Out of these 114 pregnant women presented with skin and STD. In our study, we included total 372 patients presented with dermatological specific and non-specific disorders. Most common age group presented in Raj *et al*. study was 16-30 years, in Shivakumar and Madhavamurthy 11-20 years while in our study 21-30 years.

Shivakumar and Madhavamurthy found 86 cases (50.58%) of primigravida and 84 cases (49.41%) of multigravida; in Kumari *et al*. study, out of 607 patients 303 cases (49.9%) were primigravida and 304 cases (51.1%) were multigravida while in our study we found 146 cases (39.25%) of primigravida and 226 cases of (60.75%) multigravida.

In Shivakumar and Madhavamurthy study patients were presented mostly in 3rd trimester 105 patients (61.76%), Kumari *et al*. also found most common presentation of patients during 3rd trimester 444 cases (73.1%) and our study, we found similar results 215 cases (57.80%) in 3rd trimester.

Pregnancy-specific disorders were presented; in Raj *et al*. Study 17 cases (14.91%), Shivakumar and Madhavamurthy. study 26 cases (9.41%), Kumari *et al*. study 22 cases (14.97%) while in our study 81 cases (21.77%). Prurigo of pregnancy was the most common pregnancy-specific disorder in Raj *et al*. study 14 cases (12.28%), Shivakumar and Madhavamurthy study 16 cases (9.41%) and we also found common pregnancy-specific disorder in study was Prurigo of prengnancy 40 cases (10.72%); while Kumari *et al*. study most common pregnancy-specific disorder was PUPPP 14 cases (9.52%). PUPPP was the second most common pregnancy-specific disorder in Raj *et al*. study 2 cases (1.75%) and we also found second most common pregnancy specific disorder was PUPPP 19 cases (5.11%). While in Shivakumar and Madhavamurthy study and Kumari *et al*. study second most common pregnancy-specific disorder was ICP, 6 cases (3.52%) and 5 cases (3.40%) respectively.

Among non-specific dermatological disorders in pregnancy, acne vulgaris was present in 15 cases (13.15%) of Raj *et al*. study; in 14 cases (9.52%) of Kumari *et al*. study and in our study we found 14 cases (3.76%). Eczema was present in 10 cases (8.77%) of Raj *et al*. study; in 5 cases (3.40%) of Kumari *et al*. study and in our study I found 12 cases (3.22%). Tinea was present in 16 cases (14.03%) of Raj *et al*. study; in 5 cases (3.40%) of Kumari *et al*. study and in our study I found 17 cases (4.57%). Kumari *et al* found 2 cases (1.36%) of BV while we found 22 cases (5.9%). Shivakumar and Madhavamurthy found 17.64% of patients with scabies while we found 13 cases (3.49%).

Out of all STD, VVC was the most common disorder in all studies; in Raj *et al*. study 45 cases (39.47%), Shivakumar and Madhavamurthy study 21.78%, Kumari *et al*. study 17 cases (11.56%) and we also found VVC was the most common STD in our study 58 cases (15.59%). Second most common STD in Raj *et al*. study and Kumari *et al*. study was syphilis 11 cases (9.65%) and 4 cases (2.72%) respectively;

in Shivakumar and Madhavamurthy study was T. vaginitis 8.23% while in our study was BV 22 cases (5.9%).

Raj *et al*., Shivakumar and Madhavamurthy and Kumari *et al*. were found 1 case (0.88%), 3 cases (1.76%) and 2 cases (1.36%) of HIV-seropositive respectively in their study while we found 14 cases (3.76%) of HIV-seropositive associated with pregnancy.

CONCLUSION

This study brings into focus various specific and non-specific skin disorders during pregnancy. In our study, all the dermatoses are common in young adults (21-30 years) predominantly within the 3rd trimester. The majority of women were multigravid. Prurigo of pregnancy was the most common and pruritic uricarial papules and plaques of pregnancy was the second most common pregnancy-specific disorder. Acne vulgaris was the commonest and eczema was the second most common non-specific non-infectious disorder. VVC is the most common and BV is the second most common sexual transmitted infection in pregnancy. In HIV seropositive, herpes progenitalis was the commonest disorder.

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Original Article

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Brain Space Occupying Lesions by Magnetic Resonance Imaging: A Prospective Study

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Abstract

Introduction: During the last few years, the role of magnetic resonance imaging (MRI) as a diagnostic tool in neuroradiology is well-established. With advanced MRI techniques such as perfusion, diffusion, and spectroscopy, it is now possible to differentiate between various intracranial lesions.

Aim: The aim of present study was to data analysis of brain space occupying lesions (SOL) evaluated by MRI and with histopathological correlation of patients presented with various clinical symptoms.

Materials and Methods: The study was performed on a whole body system at 1.5 Tesla MRI, using a dedicated head coil. Multiplanar T1- and T2-weighted, diffusion, gradient images, using spinecho sequences, post contrast study, and proton magnetic resonance spectroscopy were performed in all cases on single and multivoxels chemical shift imaging. All cases were correlated with histopathology and by follow-up studies after management.

Result: Study was done for a period of 1-year in patients of varying clinical symptoms subjected for MRI. SOL due to infective etiology was noted high in the age group of 10-30 years and neoplasm among 30-50 years. While glioma is the most common malignant tumor followed by matastasis and meningeoma among benign lesions as noted in previous literature. Tuberculoma was the most common lesion in the infective etiology. MRI-aided in characterizing and diagnosing uncommon lesions and tumor mimicking lesions.

Conclusion: No significant difference in 5 noted in occurrence when compared with previous study data of major brain SOL. Recent advanced MRI tests aids in characterization and narrowing differential diagnosis for brain lesions, for definitive diagnosis still histologic tissue evaluation is needed for uncommon and tumors with atypical presentation. Limitation of the study is the small group of patients, hence for image evaluation, the incidence and prevalence of rare tumors requires larger group study analysis.

Key words: Brain, Tumefactive demyelination, Tumors

INTRODUCTION

Distributions of tumor types vary substantially by age group and among the developing/developed countries. Data from several national cancer registries support differences in the epidemiology of brain tumors in children versus adults. High-grade glioma (30.5%) and meningioma (29.4%) are the most common types of adult primary brain tumors (data taken from the Swedish cancer registry). Males also generally have higher rates of primary malignant brain tumors while females have higher rates of non-malignant tumors, primary meningiomas.[1] During the last few years, the role of magnetic resonance imaging (MRI) as a diagnostic tool in neuroradiology is well-established. With advanced MRI techniques such as perfusion, diffusion, and spectroscopy, it is now possible to differentiate between various intracranial lesions. The differential diagnosis of intra cerebral necrotic tumors and the cerebral abscess is frequently difficult on conventional MRI as both can present as ring enhancing lesions.[2] The necrotic component of brain tumor (glioblastoma multiforme [GBM] and metastases) show marked hypo intensity on diffusion-weighted image (DWI) due to

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increased free water. The DWI must allow differentiation between necrotic tumors and cerebral abscess.[3] The diffusion restricted signal helps in glioma grading on the basis of increasing tumor cellularity. Magnetic resonance spectroscopy (MRS) is highly sensitive in differentiating low-grade from high-grade gliomas, perilesional tumor infiltration and more specific in characterizing abscess with lipid/lactate, amino acid peaks. Provides additional information over conventional study to differentiate extra axial tumors as meningeoma with alanine peak. Not only the common tumors are well-differentiated by MRI, but also space occupying lesions (SOL) of infective etiology, rare tumors, tumor mimicks as tumefactive demyelinating lesions and congenital lesions prevalence and imaging features are diagnosed by MRI.[4]

MATERIALS AND METHODS

The present study consisting of 53 cases of intracranial SOL for a period of 1-year attended our department for MRI evaluation for varying clinical symptoms. Among this, 50 were SOL and 3 were lesions resembling a tumor. It was a prospective study using descriptive analysis by SPSS software not applying test data analysis. The study was performed on a whole body system at 1.5 Tesla. Diagnosis of intracranial mass was confirmed by biopsy or postoperative histopathological examination, cerebrospinal fluid findings supplemented by follow-up MRI study as per clinical requirement. MRI by multiplanar T1- and T2-weighted, diffusion, gradient images, using spin echo sequences, were obtained in all the patients. For all cases, contrast study and proton MRS by single (PRESS) and multivoxel chemical shift imaging MRS was performed on 1.5 Tesla scanner (SEIMENS MAGNETOM) using 8 channel head coil with TR 2000, TE 31/144/288 with flip angle 90°. DWI is typically performed using at least two b values (e.g., b = 0 s/mm^2 and other b values from 0 to 1,000 s/mm^2) to enable meaningful interpretation.

RESULT ANALYSIS

The highest incidence of patients in the present study was found in 21-30 and 41-50 years group (16%) Table 1. Brain SOL was more common in male (64%) and in was female of 36% Table 2, which was similar as illustrated by previous study reports. Brain SOL occurs in intra axial and extra axial locations. In Table 3 shows 68% of intra axial lesions and 32% of extra axial lesions, which includes meningioma (the most common benign and extra axial neoplasm) 5th nerve schwanoma and pituitary adenoma. Intracranial SOL subjected for MRS and diffusion weighted series showed 20 cases of glioma (40%) with the highest incidence of low-grade gliomas (24%) and 8 (16%) were high-grade gliomas shows more than 50%. While low-grade gliomas (12) including ependymoma, pilocytic astrocytoma showed either no contrast enhancement (33%) or mild (in 66%) enhancement noted. Pyogenic abscess (1) and tubercular abscess (1) showed ring enhancement. All 5 cases of tuberculoma showed enhancement of variable degree. In the case of gliomas, MRS by NAA/choratio proved helpful in differentiating low-grade from high-grade gliomas with mean value in high-grade glioma is 0.28 and low-grade glioma 0.66 suggest a significant decrease in NAA and a significant increase in choline which is a marker of cell proliferation. Moreover, all cases included in this study were either surgically or by biopsy proved. Among 5 cases of metastasis 2 of known primary (carcinoma breast and lung) and 5 cases of tuberculoma were followed periodically with treatment.

Table 1: Distribution of intracranial mass lesions according to age

Patient age	No. of patients	Percentage
0-10	5	10
11-20	6	12
21-30	8	16
31-40	7	14
41-50	8	16
51-60	4	8
61-70	7	14
71-80	4	8
81-90	1	2
Total	50	100

Highest incidence of patients in present study was found in 21-30 and 41-50

Table 2: Distribution of intracranial mass lesions according to sex

Sex	No. of patients	Percentage
Male	32	64
Female	18	36
Total	50	100

Table 3: Distribution of intracranial mass lesions according to location

Location	No. of patients	Percentage
Intra axial	34	68
Extra axial	16	32
Total	50	100

Present study showed more incidence of intra axial lesions (68%)

DISCUSSION

Patients with brain SOL presented with one or more symptoms that include seizures, increased intracranial

pressure, or localized neurologic deficits such as weakness, motor problems, and aphasia. Brain SOL has wide spectrum of lesions such as infective, vascular, and benign and malignant neoplasm. Infective lesions include granulomatous lesions and pyogenic abscess. Common benign lesions are predominently extra axial such as meningeomas, pituitary adenoma, schwanoma and less common tumors as epidermoid, and hemangioma chordoma. Glioma and metastasis are the common malignant neoplasms of the brain. Multiple lesions denote metastasis or infective etiology, whereas multifocal glioma are rare, and in present study 92% of SOL were solitary and 4 of 50 cases were only multiple (2) metastasis and (2) tuberculoma (Table 4). Among 53 cases, 50 were SOL in the present study group, 3 were tumor-like lesions (Table 5) and 40% was glioma as compared with of 80% by Ostrom *et al.*[5] Low-grade gliomas including oligodendoglioma, astrocytoma, and ependymoma constitute 15-18%,[6] which was 24% in our study. In the largest stereotactic brain biopsy series, the most common intra axial brain masses were high-grade primary neoplasms 36%, low-grade primary neoplasms (33%), metastases (8%), demyelinating and inflammatory conditions 3%, and abscesses 1% by Al-Okaili *et al.*,[2] which is variable with our analysis of meningeoma of 16% and infective and metastasis of significant in number 10% each. High-grade gliomas have low survival rate, as GBM represents the most common type of glioma as by other studies,[2,5,7] it was falling next to low-grade in our series.

Tumors of the central nervous system are graded according to WHO, are graded based on standard histopathological features as atypical cells, mitoses, endothelial proliferation, and necrosis. Grades I and II gliomas were taken together as low-grade, and Grades III and IV were considered high-grade gliomas. On contrast MRI study, some astrocytomas and virtually all oligodendrogliomas do not contrast enhance, and even the high-grade astrocytomas that do contrast enhance frequently show enhancement in only a portion of the tumor. Because these tumors have abnormal T2 transverse relaxation time that is difficult to distinguish from surrounding edematous but otherwise normal brain tissue (Figure 1). MRS was useful in the perilesional spread of the tumor infiltration in high-grade gliomas and recurrent tumors.[8] In present study, 8 cases of low-grade gliomas (66.66%) and all case of high-grade gliomas (100%) showed pathological spectra not limited to contrast enhancing area. On MRS Naa/ch ratio was significantly lower and ch/cr ratio was significantly higher in high-grade gliomas than in low-grade gliomas.

Meningiomas occur at a rate of 7.8 per 100,000 per year, but only 25% are believed to be symptomatic.[9] Meningiomas typically appear as extra axial lesions, and the presence of a dural tail aids in the diagnosis. While meningeomare present 16% in the present study as compared to 33% incidence of brain tumors by Wiemels *et al.*[10] Among 8 cases of meningeoma, 1 case of malignant meningeoma occurred in male (Figure 2) rest of 7 were noted in the female. Computed tomography can help evaluate bone involvement and the presence of calcifications, which can be seen in 30% of benign meningiomas[10] but are rare in malignant meningiomas**.** Although benign tumors showed perilesional edema, it was much more in malignant meningiomas. Meningiomas could be differentiated from schwannomas by the presence of alanine in the former. All cases of meningeoma showed moderated to intense enhancement with T2 hypointensity; diffusion restricted

Table 4: Distribution according to number of intracranial mass lesions

Number of lesions	No. of patients	Percentage
Single	46	92
Multiple	4	8
Total	50	100

Present study found more incidence of solitary as compared to multiple lesions (92%)

Table 5: Distribution according to histopathalogy of intracranial mass lesions

Type	No. of patients	Percentage
Low-grade glioma	12	24
High-grade glioma	8	16
Metastases	5	10
Meningioma	8	16
Schwannoma	1	2
Pyogenic abscess	1	2
Tubercular abscess	1	2
Medulobla stoma	2	4
Piueoblastoina	1	2
Tuberculoma	5	10
Pituitary macroadeuoma	6	12

Figure 1: Glioma in the frontal lobe appears hyperintense on T2 series that is difficult to distinguish from surrounding edematous but otherwise normal brain tissue

signal and Ch, Alanine peak on MRS. All metastases and meningiomas (100%) showed pathological spectra limited to contrast enhancing area in our study. Pituitary macro adenoma (6 cases) (Figure 3) also showed increased Ch peak. Lactate and lipid peak was noted on all extra axial tumors including 8th nerve schwanoma (Figure 4). However, no significant MRS or diffusion features noted for pineoblastoma (Figure 5) where anatomical localization and enhancement features aided in diagnosis.

Metastasis to the brain occurs in 20-40% of known primary tumors and the most common (40%) intracranial tumor in adults. Lung, breast, and melanoma are the most common primary tumors to metastasize to the brain. Most commonly, the metastatic disease affects the skull or brain parenchyma and also involve the meninges.[11] In present study, 2 out of 5 cases were multiple lesions (Figure 6) with disproportionate perilesional edema showed mild to moderate contrast enhancement. A single case of solitary

Figure 2: Case of recurrent malignant meningeoma shows intense enhancement with areas of necrosis, perilesional edema, and meningeal enhancement

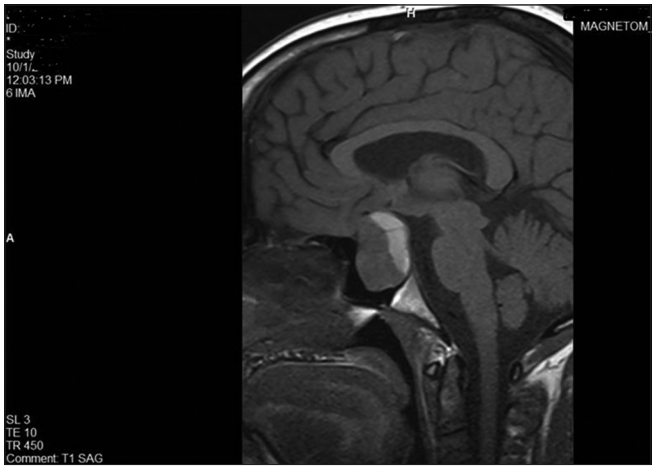

Figure 3: Pituitary macro adenoma with mixed signal intensity with figure of eight

Figure 4: Posterior fossa lesion with central necrosis with mild enhancement of the solid component in a case of 8th nerve schwanoma

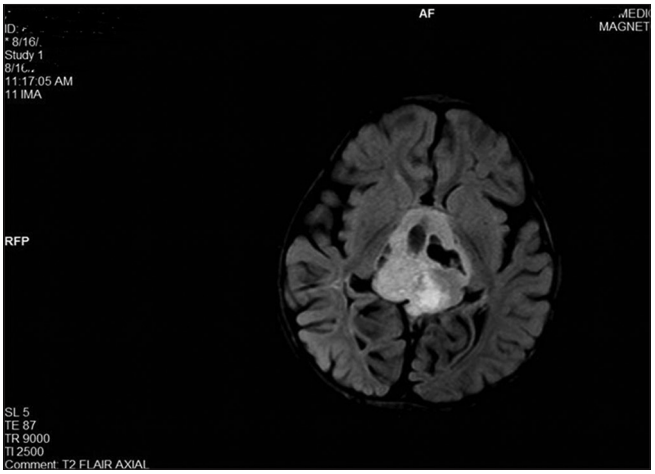

Figure 5: Pinealoblastoma with calcification, intense enhancement and necrosis with no characteristic study pattern on magnetic resonance spectroscopy

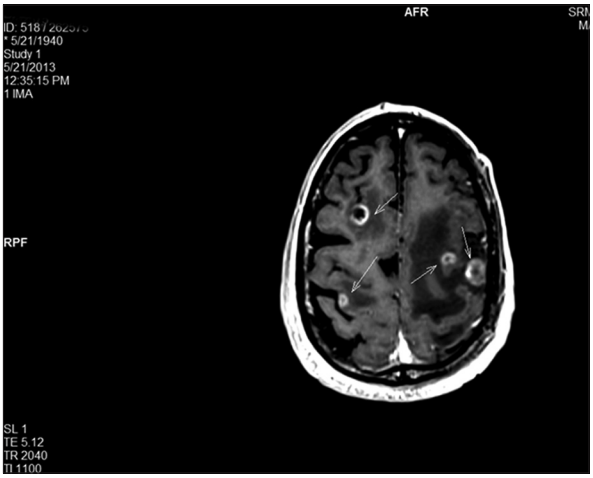

Figure 6: Multiple ring enhancing lesion with perilesional edema without diffusion restricted signal and elevated ch/cr ratio denoting multiple metastasis

metastasis showed necrosis and was not able to differentiate from glioblastoma on with MRS, which showed elevated ch/cr (4), lipid/lactate (4) peaks with NAA/Cho > 1 in peritumoral edema.

Non-neoplastic lesions including intracranial abscess, granuloma, phakomatosis, and tumefactive demyelination can cause a diagnostic dilemma. 3 cases of brain lesions of the present study were mimicking brain SOL, as tumefative demyelination (2 lesions), phakomatosis (1 lesion). Tubercular and pyogenic abscess showed ring enhancement with lactate/lipid peak and diffusion restricted signal. Tumefactive demyelination diseases, of multiple sclerosis, acute disseminated encephalomyelitis may present as tumor-like lesions on imaging. By MRI abscess displaying solitary or multiple focal areas of signal alteration with peripheral ring enhancement. Among 2 cases of abscess, in present study, 1 case (tuberculus abscess) showed multiple lesions widening the spectrum to include metastasis as well. Both showed irregular, incomplete open ring enhancement with central necrosis closely resembling glioblastoma causing difficulty in differentiating. MRS in tumefactive demyelination showed a reduction of NAA and increased in choline and lipids, and elevation of lactate due to ischemia.[12] However, these resonance spectra are not specific, and they may resemble brain tumors or even tuberculoma.

CONCLUSION

Detailed information of brain lesions by MRI aid in diagnosing and management. More over, Noninvasive recent advanced MRI techniques plays a major role in characterization and narrowing differential diagnosis for brain lesions, still for definitive diagnosis histologic tissue evaluation is needed for uncommon and lesions with the atypical and overlapping presentation. Limitation of the study is the small group of patients, hence for image evaluation, the incidence and prevalence of rare and tumors like lesions require larger group study analysis in future which forms one-third of brain SOL.

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Original Article

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Rickettsial Diseases: A Study Evidenced by Weil-Felix Test in a Tertiary Care Hospital

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Abstract

Background: Rickettsial diseases are among the most obscured re-emerging arthropod borne zoonotic infections that are being increasingly recognized as one of the causes of pyrexia of unknown origin (PUO). Presenting with varied and non-specific symptoms, ignorance and low index of suspicion, they are often under diagnosed due to the unavailability of the reliable diagnostic test. Appropriate diagnosis in early stages is necessary to prevent the morbidity and mortality associated with these infections.

Objective: Present study attempts to understand the scenario of rickettsial infections causing acute febrile illness and to categorize rickettsial disease titers by Weil-Felix test (WFT) in our tertiary care hospital.

Materials and Methods: A total of 133 cases with acute undifferentiated fever were included in the study. These samples were subjected to qualitative slide agglutination and quantitative tube agglutination by WFT and interpreted along with clinical data.

Results: A total of 29 out of the 133 cases (21.8%) tested positive for rickettsial infections by the WFT. Out of 29 cases, 16 (55.17%) were seropositive for scrub typhus, 3 (10.34%) for spotted fever, and 2 (6.89%) for typhus fever. The remaining 8 (27.58%) samples showed mixed titers.

Conclusion: In view of its significance in timely diagnosis, treatment, and prevention of life-threatening complications in clinically compatible cases of PUO, WFT should not be disregarded as this test can be easily set up with a moderate level of infrastructure and expertise.

Key words: Rickettsial diseases, Scrub typhus, Spotted fever, Typhus fever, Weil-Felix test

INTRODUCTION

The family Rickettsiaceae encompasses obligate intracellular rods belonging to the subgroup Alphaproteobacteria. The members of this family are aerobic Gram-negative non-flagellate pleomorphic *Coccobacilli* adapted to parasitize ticks, lice, fleas, mites, chiggers, and mammals. Family Rickettsiaceae comprises of the following genera - *Rickettsiae, Ehrlichia,* and *Orientia*. These zoonotic pathogens cause infections that disseminate in the blood to many organs.[1] Rickettsial diseases have been documented in India since the 1930s; many cases have been reported from Madhya Pradesh, Maharashtra, Karnataka, Tamil Nadu, Kerala, Jammu and Kashmir, Himachal Pradesh, Uttaranchal, Rajasthan, West Bengal, and Assam.[2-4]

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Rickettsial diseases are veiled re-emerging infections, which pose a serious threat to public health if not meticulously diagnosed. Rickettsial infections are enlisted among the etiological factors attributed to cause pyrexia of unknown origin (PUO) and thereby require to be differentiated from other febrile illnesses such as enteric fever, malaria, dengue, leptospirosis, and infectious mononucleosis.[5] The lack of data regarding geographical distribution and the low index of suspicion due to non-specific clinical manifestations poses a challenge to the physician and hinders the diagnosis.

Tests available to diagnose rickettsiosis are culture, serology including immunofluorescence, and molecular tests. Culture is extremely strenuous, hence impractical

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for routine diagnostic application. Except serological diagnosis, other tests are beyond the reach of most diagnostic laboratories.[6] Serological tests, such as Weil-Felix test (WFT), latex agglutination, indirect hemagglutination, immunoperoxidase assay, Enzyme Linked Immunosorbent Assay (ELISA), and micro immunofluorescence ("gold standard"), can be used in laboratory evaluation of suspected rickettsial infections.[7] Many cross-reactions are observed, and explicit species determination of the infecting agent is difficult. Western blot may be more specific in early sera. Cross-absorption may help to resolve the problem of cross-reaction, but it is technically demanding and expensive. Nested polymerase chain reaction (PCR) is the standard molecular diagnostic method for testing of blood and fresh tissue specimens at the centers for disease control and prevention.[8] Real-time quantitative PCR and nested PCR are targeted at the gene encoding the major 56 Kda and/or 47 Kda surface antigen gene, which is valuable in serum testing of rickettsial diseases.[1]

The present study was undertaken in our tertiary care institute with the intention to present the scenario of rickettsial infections as a cause of PUO. In the present study, we have used WFT in the diagnosis of rickettsial infections. WFT is a non-specific heterophile tube agglutination test in which antibodies against rickettsiae are detected using a heterophile Proteus antigen.

MATERIALS AND METHODS

A prospective hospital-based study was conducted in the Department of Microbiology of a teaching hospital between February 2014 and March 2015. The total of 133 patient samples were included in the study.

Inclusion Criteria

Patients hospitalized with undiagnosed fever; presenting with one or more of the following clinical features: Rash, edema, hepatospenomegaly, lymphadenopathy, eschar, and tick or flea exposure were included in the study.

Exclusion Criteria

Patients treated on outpatient basis and patients with a known cause of fever at the time of admission were excluded from the study.

After following proper aseptic precautions, each patient's blood was collected in a sterile vacutainer by venipuncture in the laboratory. The patient's blood sample was centrifuged and the serum thus obtained was subjected to WFT (PROGEN, Tulip diagnostics Pvt. Ltd.) tested by qualitative slide agglutination and quantitative tube agglutination test according to standard protocols with doubling dilution of 1:20-1:160, for initial screening followed by further dilutions to achieve end titer.[8] Positive samples were also correlated with other tests like Widal test, Dengue IgM ELISA and the presence of Proteus infection by urine culture of the patients. Statistical calculations were done using percentage analysis and Chi-square test.[9]

RESULTS

Based on the baseline titer of rickettsial diseases in this geographical area, OX-K, OX-19, and OX-2 titers of 160 and above were considered significant.[5]

Out of 133 samples, 32 blood samples showed slide agglutination. 3 samples tested positive qualitatively by slide agglutination but were negative by tube agglutination; hence, they were considered equivocal, and the test was repeated using fresh serum samples from the respective patients after 1 week and confirmed to be negative. The 29 (90.62%) of 32 samples were regarded significant based on titers obtained by tube agglutination test. Out of 29 significant titers, 16 (61.53%) samples were significant for OX-K antigen and thus for scrub typhus.

The significant titers for OX-2 and OX-19 were 12 (41.37%) and 5 (17.24%), respectively (Table 1). Based on OX-2 and OX-19 titers 3 samples were suggestive of spotted fever (9.3%), 2 samples suggestive of typhus fever (6.25%), and 8 samples yielded mixed titers (25%) making it difficult to interpret the results (Table 2).

Age-wise analysis of the positive cases evidenced 8 cases in pediatric age group (0-12 years), 2 cases in adolescent (13-20 years), 16 cases in adult (21-64 years), and 3 cases in elderly (>65 years) age group with $P = 0.0007$ (Figure 1).[10] Among 29 samples, 20 (68.96%) were males and 09 (31.03%) were females with $P = 0.041$ (Figure 2).

Table 1: Titers obtained by Weil-Felix tube agglutination

Titers	1:640	1:320	1:160
OX-K	2	7	7
OX-2	-	4	8
OX-19	2	2	1

Table 2: Split up of the titers obtained

OX 19	OX 2	OX K	Number	Diagnosis
-	-	Positive	16	Scrub typhus
Positive	Positive	-	3	Spotted fever
Positive	Positive/negative	-	2	Typhus fever
Positive/negative	Positive/negative	-	8	Mixed titers

All the seropositive patients presented with fever among whom 55% had rashes; 27% had hepatomegaly, and 20% had splenomegaly. Table 3 explains the relationship between clinical presentation and test positivity.

Among the samples showing mixed titers, only one sample was positive for Salmonella, and two samples were positive for dengue (Table 4). Dengue IgM was detected by ELISA. Dengue PCR to confirm the diagnosis could not be done due to lack of availability. The Widal positive sample showed titers of 1:160 for Typhi O and H and <1:80 for paratyphoid AH and BH. Blood culture for isolation of typhoid bacilli was performed on this Widal positive sample by using automated BACTEC 9050, and it turned out to be negative. All the patients tested negative for urine Proteus.

DISCUSSION

In recent years, Rickettsial diseases are one among the re-emerging radices of acute undifferentiated febrile illness in several parts India.[11-13] India being a developing country; there is scarce data and insufficient research on rickettsial diseases. The clinical diagnosis of Rickettsial diseases is intricate and cumbersome. Laboratory culture of this organism is not endorsed due to high chances of laboratory-acquired infections to the handling personnel. Therefore, the diagnosis of rickettsial infections depends on serological and molecular diagnostic techniques. Serological tests include latex agglutination, immunofluorescence, indirect hemagglutination, ELISA, and WFT.[4] Molecular diagnostic techniques, such as the PCR for detection of rickettsial DNA although available, are not realistic due to cost related issues.

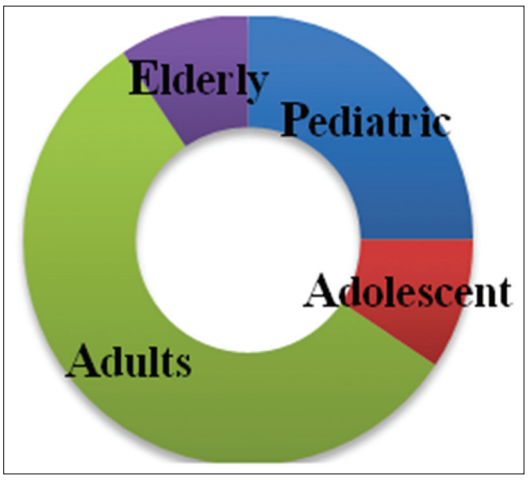

Figure 1: Age-wise split up of patients with significant titers (*P* = 0.0007)

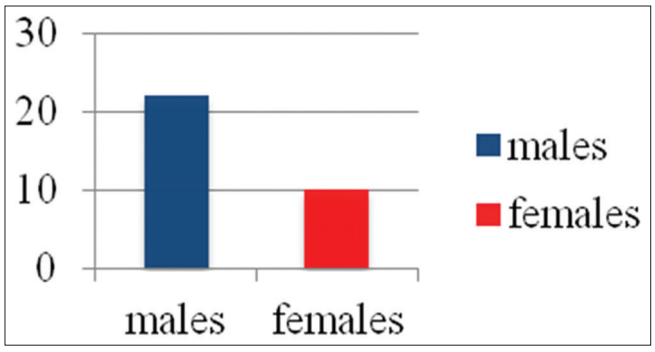

Figure 2: Male:female ratio of patients with significant titres (*P* value = 0.041)

WFT depends on a fortuitous similarity of certain carbohydrate antigenic determinants, which occur in most species of pathogenic rickettsia species and in the OX-19, OX-2 and OX-K strains of *Proteus vulgaris* and *Proteus mirabilis*.[9] The test has too many stumbling blocks, and irrelevant results can be seen in many other conditions. False positive results have been obtained in cases with Salmonellae, *Streptococcus pyogenes*, and Proteus infection.[14] The importance of this test, though being not a standard test, is still reasonably good when it comes to evaluating pyrexia of unknown origin (PUO). In the present study, the agglutination of OX-2 and OX-19 were seen in 12 (41.37%) and 05 (17.24%) patients, respectively. Agglutination of OX-K was seen in 16 (55.17%) patients.

WFT, when performed in conjunction with other tests, such as Widal, Dengue IgM ELISA, and urine culture for Proteus infection, can eliminate the false positive cases. In the present study, out of 29 positive samples, only three were positive for typhoid and dengue; however, false positivity could not be entirely ruled out due to the absence of a specific test.

Table 3: Clinical features in patients with positive WFT

Clinical features	Number of cases
Fever	29
Hepatomegaly	9
Splenomegaly	6
Rash/eschar	16

WFT: Weil-Felix test

Table 4: Tests done to rule out other causes and check the correlation with WFT

Tests	Number of samples (*n*=29)	
	Positive	Negative
Widal	01	28
Dengue IgM test	02	27
Proteus isolation	00	29
Chikungunya	00	29
Leptospira	00	29
Malaria	00	29

WFT: Weil-Felix test

Figure 3: Eshcar in a scrub typhus patient

Undiagnosed fever was the major inclusion criteria for the study. The other symptoms associated with fever also played a role in clinical suspicion towards a diagnosis of rickettsial infections. Among the 133 patients tested as part of the study, rashes and eschars were seen in 16 of the 29 Weil-Felix positive cases (55.17%). Figure 3 shows a typical eschar which was found on the cheek of a 48 year old female patient with OX-K titre of 1:320 and OX-2, OX-19 titres less than 1:80. However, all patients showing a positive WFT did not show a characteristic rash. We noticed that 09 patients who had fever and rash showed the negative result with WFT. A study by Udayan *et al.* showed 61.7% association[7] and a study by Mittal *et al.* showed 51.7% association of rashes with positive WFT.[5] Hepatomegaly was evidenced by 9 patients who showed OX-K levels >1:320. This was in correlation with the study by Udayan *et al.*[7] However, only 6 of these patients showed splenomegaly.

Failure in early diagnosis is associated with significant mortality and morbidity. The fulminant course of rickettsial infections can lead to life-threatening manifestations such as disseminated intravascular coagulation, meningoencephalitis syndrome, acute renal failure, hepatic failure, non-cardiogenic pulmonary edema, interstitial pneumonitis, and myocarditis.[4] The therapy is affordable and yields dramatic results when diagnosed early in the course of the disease. Epidemiological features, history of exposure to vector, and a high index of suspicion are crucial aids toward accurate diagnosis.[4,5]

CONCLUSION

Persistence of fever even after 48 h, the presence of rash and tick exposure with altered biochemical parameters should alert the clinician toward rickettsial diseases. Rickettsial diseases can cause severe illness and even death in otherwise healthy adults and children; however, if timely treatment with doxycycline or third generation cephalosporins is instituted the adverse consequences can be well averted.

Thus, when proper precautions are taken with respect to the use of standardized antigen and inclusion of positive serum controls, the WFT can help in establishing the presumptive diagnosis of rickettsial disease. When this is teamed alongside with clinical correlation of patient's signs and symptoms, there can be successful, cost-effective diagnosis and treatment.

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Original Article

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Cytological Evaluation of Thyroid Lesions and its Correlation with Histopathology: A Prospective Study

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Abstract

Introduction: Fine-needle aspiration cytology (FNAC) has an important role in differentiating between neoplastic and non-neoplastic lesions of the thyroid. It is a quick outpatient department (OPD) procedure. It greatly affects the treatment decision. The current study was carried out to evaluate the role of FNAC as a diagnostic tool in thyroid lesions and establish a clinico-cytological, biochemical, and histological correlation.

Purpose: The purpose of this study is to establish a cytohistological correlation in thyroid lesion and to find out can FNA obviate the need for histopathological diagnosis in thyroid lesions.

Materials and Methods: It is a prospective study of thyroid lesions carried out at the Department of Pathology, Government Medical College, Srikot, Srinagar Pauri Garhwal Uttarakhand over a period of 2-year. A total of 136 patients with thyroid lesion were undertaken for FNAC. Their clinico-cytological, biochemical, and histological correlation was done. Their statistical analysis was done.

Results: Majority of the cases were non-neoplastic. The accuracy of cytodiagnosis was 94%.

Conclusion: FNAC of thyroid lesion has a high accuracy in differentiating between malignant and benign lesions. It is safe cost effective, minimally invasive, and OPD procedure. Using FNAC as the first line of investigation, the number of surgeries for thyroid lesion has reduced greatly.

Key words: Accuracy of fine-needle aspiration cytology, Histopathology, Sensitivity, Specificity

INTRODUCTION

Thyroid fine-needle aspiration cytology (FNAC) was introduced in 1950 and became popular worldwide in 1980.[1] Today, it is a well-established technique for pre-operative diagnosis of thyroid pathologies. Thyroid lesions may cause sign and symptoms of hypothyroidism or hyperthyroidism and also have malignant potential.[2] Therefore, accurate evaluation of thyroid lesions is difficult.

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Various non-invasive methods used for diagnosis of thyroid lesions do not make a definitive diagnosis of malignant lesions. FNA has now replaced most other tests used for pre-operative diagnosis of thyroid lesions. Now-a-day, most clinicians rely solely on FNA for making a diagnosis of benign lesions. As a result the incidence of malignancy in thyroidectomy patients has increased from 10% to 30-50% in recent years.[3] In spite of the first choice of investigation in thyroid lesions, it also has some limitations. The reported pitfalls are mostly related to sampling techniques, the skill of doctor performing the aspiration, sample adequacy, the experience of pathologist interpreting the aspirate, and overlapping cytological features between benign and malignant follicular neoplasm.[4,5]

FNAC is safe relatively simple and cost effective for evaluation of thyroid patients. This procedure provides

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a tool for detecting thyroid malignancies in an early stage, resulting in a better outcome of patients. In this study effectiveness of FNAC is evaluated in the clinical management of thyroid disease and also to reduce the rate of surgery in benign cases.

MATERIALS AND METHODS

This is a prospective study of thyroid lesions carried out at Department of Pathology, Government Medical College, Srikot, Srinagar, Pauri Garhwal, Uttarakhand over a period of 2-year (June 2013 to May 2015). Patients from ENT outpatient department (OPD) and from medicine OPD were taken for FNA. 136 FNACs were done during this period. Patients of all ages and both the sexes were included in the study. Out of 136 patient, histological confirmation was available in 52 cases. A sample of histopathology was collected from our own surgical department as well as from the surgeries done outside. Methods used in this study included a clinical presentation, thyroid function test, FNAC, and histopathology. Sign and symptoms related to thyroid gland were a solitary nodule, multinodular, and diffuse goiter. Sign of compression, hoarseness of voice, cough, pain, dysphagia, and symptoms related with hypo functioning or hyper functioning of thyroid gland. Thyroid function test was used to determine the level of free T3, T4 and free T4, and thyroid stimulating hormone.

All FNA was done by the pathologist as the outpatient procedure; no ultrasound guided FNA was done. Air-dried smears were stained with May–Grunwald–Giemsa, and wet smears were stained with papanicolaou and hematoxylin and eosin stain. The results of FNAC were compared with histopathology in 52 cases. The cytological results were also correlated with clinical features and thyroid function test. The statistical analysis included sensitivity, specificity, accuracy, false positive rate, and false negative rate.

RESULTS

FNAC performed in 136 patients of which 82% were female, and 18% were male. Most of the patients were in the age group of 20-40 (Table 1). Most common presenting symptom was painless solitary nodule (Table 2). Among 136 patients, 81.6% were non-neoplastic, and 18.4% were reported as neoplastic on cytology (Table 3, Figures 1,2)). Cytohisto-correlation was done in 52 cases. 49/52 cases were confirmed on histology (Figures 3 and4), one was false positive and two were false negative (Table 4). The sensitivity of FNAC was 90%, specifitive was 96% (Table 5).

Table 1: Age distribution of thyroid patients

Age group in years	Number of patients
0-20	14
21-40	70
41-60	40
61-80	12
Total	136

Table 2: Clinical sign and symptoms

Clinical sign and symptoms	Number of patients
Goitre	136
Solitary nodule	111
Multinodular	17
Diffuse	08
Pain	10
Dysphagia	08
Hoarseness	12
Cough	03
Sign and symptoms of increased hormonal concentration	10
Sign and symptoms of decreased hormonal concentration	12

Table 3: FNAC of thyroid nodule (*n*=136)

Non-neoplastic lesions	*n*=111
Nodular goiter	62
Benign cyst	24
Thyroiditis	25
Neoplastic lesions	*n*=25
Follicular neoplasm	14
Papillary neoplasm	06
Hurthle cell neoplasm	04
Anaplastic	01
Total	136

FNAC: Fine-needle aspiration cytology

Table 4: Cytohistological correlation (*n*=52)

FNAC	Histology		Total
	Neoplastic	Non-neoplastic	
Neoplastic	19	1	20
Non-neoplastic	2	30	32
Total	21	31	52

FNAC: Fine-needle aspiration cytology

Table 5: Statistical analysis (%)

Sensitivity	90
Specificity	96
False positive rate	3.1
False negative rate	9.1
Accuracy	94

DISCUSSION

Thyroid enlargement is the most common occurrence in the sub-Himalayan region of the India. Our hospital

is located in Garhwal region. This hospital gets patients exclusively from this region. These regions are iodine deficient areas. The incidence of goiter is much higher in these regions. Thyroid enlargement whether nodular or diffuse needs thorough investigation, mainly to rule out malignancy or thyroiditis. Thyroid malignancy accounts for 1% of all malignancy. Early diagnosis of thyroid cancer provides higher life expectancy due to low malignant potential and slow progressing nature of thyroid cancer.

FNAC has excellent patient acceptance and no morbidity. It is easy and low-cost effective test used in the diagnosis of the thyroid nodule.[4,6,7] FNAC of thyroid nodule has decreased the rate of thyroid surgery while increasing the percentage of malignancy in thyroidectomy patients.[8]

The value of any test depends on its ability to detect the presence of disease (sensitivity) and to verify the absence of disease when it is not presence (specificity). The sensitivity of thyroid FNAC ranges from 74% to 92% and specificity ranges from 74% to 100%.[9,10] In our study, sensitivity was 90%, and specificity was 96%, which correlates with other studies.[11,13-18] This shows that FNAC is more specific than sensitive. The reason for the wide range of sensitivity and specificity is the difference in the way of categorization of lesions by a different cytopathologist.

Factors that reduce the efficacy of FNAC of thyroid include inadequate sampling, the inexperience of cytopathologist, and difficulty in differentiating between benign and malignant follicular lesions. Inadequate sampling may result from sclerotic, calcified nodule, or nodule with cystic degeneration in large areas.

The solitary thyroid nodule is less likely to be malignant. In our study, of 111 patients of solitary nodule, only six were reported as neoplastic on FNAC. Which correlates with others studies.[12,13]

Most common age group in our study was the 3rd and 4th decade of life, which is accordance to the study of

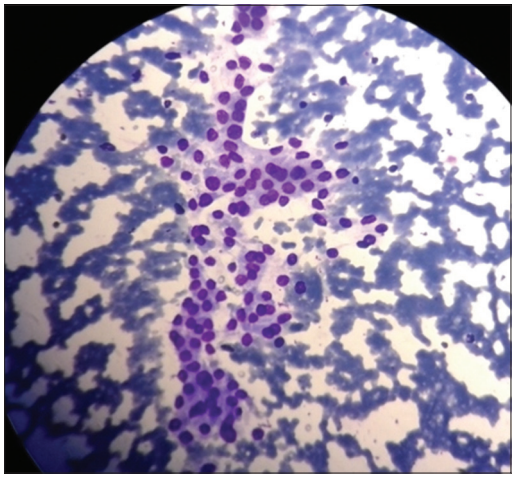

Figure 1: Papillary structure in papillary carcinoma on fine-needle aspiration cytology (×10)

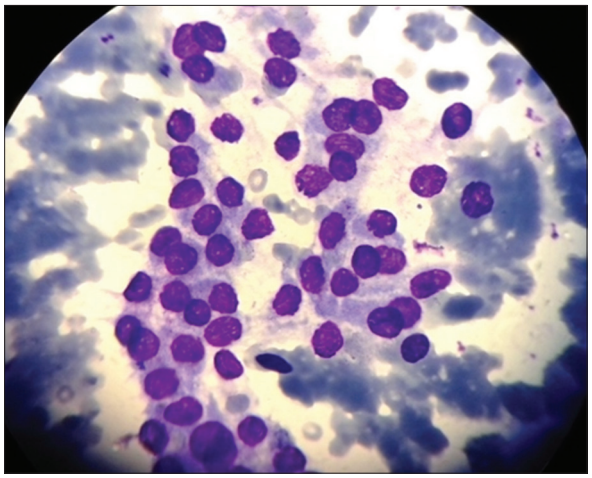

Figure 2: Anisonucleosis and nuclear grooveing in papillary carcinoma on fine-needle aspiration cytology (×40)

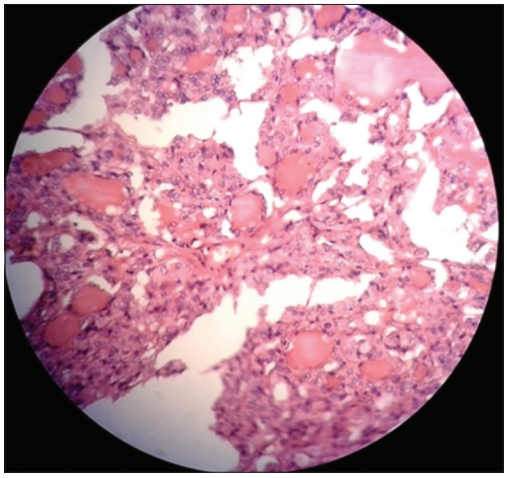

Figure 3: Papillary carcinoma on histology (×10)

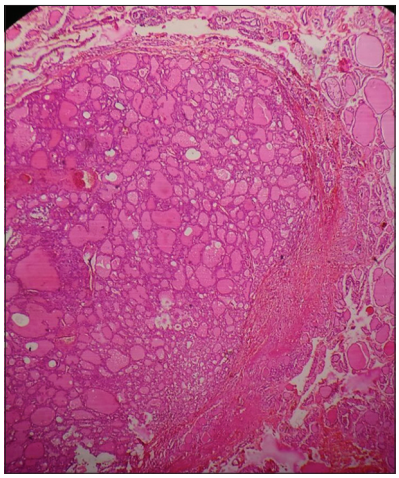

Figure 4: Capsular invasion in follicular carcinoma (×40)

Bukhari *et al*. and Khanzada *et al*. Most of the malignant patients presents after 5th decade of life. Anaplastic carcinoma which is usually seen in late ages, in this study, the age of anaplastic carcinoma was 39 years.

In our study, there was 106 female and 30 male, with a male to female ratio of 1:3.5 which correlates with the study of Sharma.[19] In this study, rate of false negative was 9.7% and false positive rate was 3.1% which was accordance with the study of Sharma.[19] In previous studies, false negative rate were reported between 1% and 7% and false positive rate 1-11%.[4,7,9] Wide range of false negative and false positive may be due to sampling error and cytological interpretation. False negative FNAC occurred in two cases. Both cases were diagnosed as adenomatoid goiter on histopathological examination both were confirmed as follicular carcinoma. False positive was only one case which was diagnosed as Hurthle cell neoplasm on cytology, but on histology it was confirmed as Hurthle cell change in hyperplastic goiter.

CONCLUSION

FNAC is rapid, simple, cost-effective, and minimally invasive diagnostic tool for making pre-operative assessment of patient with the thyroid nodule. By adopting this method, unnecessary thyroid surgeries for benign lesions can be avoided.

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Original Article

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Histopathological Study of Prostatic Diseases in Garhwal Region

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Abstract

Introduction: Prostatic pathology is one of the commonest disorders causing considerable morbidity and mortality in elderly male population. Benign prostatic hyperplasia (BPH), prostatitis and prostatic cancer are the most common pathological processes affecting prostate. As there has been very little study, if any, carried out on prostatic pathology in Garhwal region, hence we conducted this study on patterns of prostatic diseases based on histopathological specimens. This study can help us to determine various histopathological growth patterns of benign prostatic hyperplasia, age distribution of various prostatic lesions and grading and scoring of prostatic carcinoma according to Gleason system.

Purpose: To study the pattern and incidence of different prostatic disorders in Garhwal region.

Methods: A retrospective study, over a period of five years, was carried out on the material which included the histopathology slides and the tissue blocks and relevant clinical data was obtained from the department of pathology.

Results: BHP was the commonest encountered lesion seen in the prostate (92.6%) and was on many occasions associated with prostatitis. Fibromyoadenomatous pattern was seen to be the most commonest growth pattern of BHP. Prostatic adenocarcinoma was found in about 7.4% of all cases and majority of these cases were of high grade adenocarcinoma and were of Gleasons score 7-9.

Conclusion: In our study in Garhwal region, Benign prostatic hyperplasia came out to be the commonest prostatic disorder and prostatic adenocarcinoma was the commonest variant of prostatic cancer.

Key words: Benign prostatic hyperplasia, Prostate, Prostatitis, Prostatic adenocarcinoma

INTRODUCTION

Prostatic lesions have been on an increase over the past few decades due to higher life expectancy and an ever increasing population in the 6th, 7th, and 8th decades of life. Diseases of prostate caused significant morbidity and mortality in adult males throughout the world, though with varying incidence in various geographical areas. The prostate is affected by a variety of pathological processes, but the more frequent encountered are Benign hyperplasia prostate (BHP), prostatitis, and prostatic cancer. BHP is the most common urological disorder in males beyond 40 years age. The clinical incidence of this disease is only 8% during the 4th decade but it reaches 50% in the 5th decade and 75% in the 8th decade of life.[1] Advanced age and an intact androgen supply are the only undisputed risk factors for BHP.[2] Prostatic cancer is one of the most common malignancies affecting men worldwide, and in certain regions, even is the most common. In certain autopsy studies, the prevalence of the disease is approximately 30% in men older than 50 years, while foci of adenocarcinoma has been found in virtually all men older than 90 years.[3] Prostatic adenocarcinomas constitute more than 95% of total prostatic malignancies and hence is the most common variant of prostatic malignancies by a fair margin. Prostatitis is another common urinary tract associated problem for men younger than 50 years age

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and third most common urinary tract problem for men older than 50 years age.[4] The aim of the current study was to determine the various histopathological patterns of the prostatic lesions, in our region, where very rarely such studies have been undertaken. Furthermore growth patterns of BHP and grading and scoring of prostatic adenocarcinomas according to Gleasons system was done.

MATERIALS AND METHODS

The present study was a hospital based retrospective study carried out in the Department of Pathology, Vir Chander Singh Garhwali Government Medical Science and Research Institute, Srinagar, Garhwal, Uttarakhand. The materials for the study included histopathology slides, and tissue blocks of all the prostatic specimens received between January 2010 and August 2015. The relevant clinical history and data was also taken from the Pathology Department files, and was present in all cases. The hematoxylin and eosin (H and E) stained slides were retrieved and the slides were reviewed using light microscope under various magnifications, and the various histopathological findings were noted. Fresh sections were taken from tissue blocks in some cases, wherever required, and were stained with H and E stain. The various lesions of prostate were noted down. The various morphological types of BHP were described according to classification given by Franks.[5] The tumors were classified according to WHO classification[6] and the histological grading of adenocarcinomas was done as per the Gleasons system.[7] Data were then analyzed using tables, figures and percentages.

OBSERVATIONS

A total of 92 prostatic lesions were recorded during the time period spanning from January 2010 to August 2015. All the relevant data including ages of patients were recorded. Out of the total of 92 prostatic specimens, 88 were prostectomy specimens while 4 were prostatic biopsy specimens. The prostectomy specimens were grossly gray-white to gray to tan in color, globular to nodular in appearance, and ranged in size from 2.5 to 13 cm in diameter. The consistency of these gross specimens varied from firm to hard. The cut sections of most of these specimens were homogenous, except two cases where there was well-defined growth within the gross specimen, which later on turned out to be prostatic carcinoma. The four prostatic biopsy specimens were narrow strips of gray-white tissue ranging in length from 0.5 to 1.5 cm. The histological features and the histopathological diagnosis of each case were also noted down. The prostatic lesions were broadly classified into BHP, prostatitis, prostatic intra-epithelial neoplasia and prostatic cancer. In our study, BHP was found out to be the most common lesion affecting 85 (92.4%) cases. Prostatitis was divided into acute, chronic and granulomatous types and many of these were seen in association with BHP or prostatic cancer. Chronic prostatitis was found out to be the most common inflammatory lesion, followed by chronic prostatitis and granulomatous prostatitis. Granulomatous prostatitis was seen in only one case and was associated with a case of BHP. Prostatic cancer was seen in 7 (7.6%) cases and all of these cases were of prostatic adenocarcinomas.

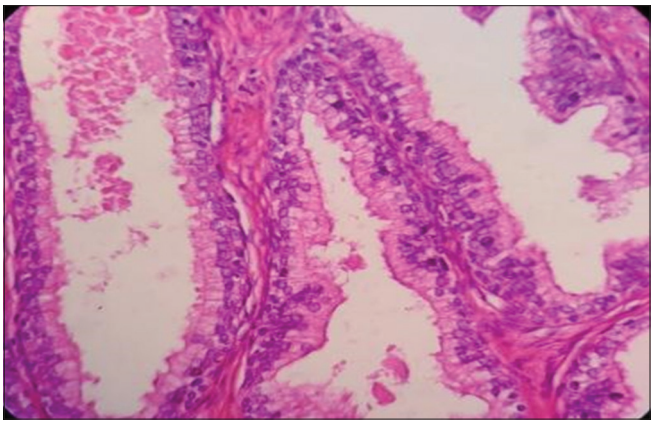

Figure 1: Typical bilayer of cells in a case of benign hyperplasia prostate (H and E stain, ×400)

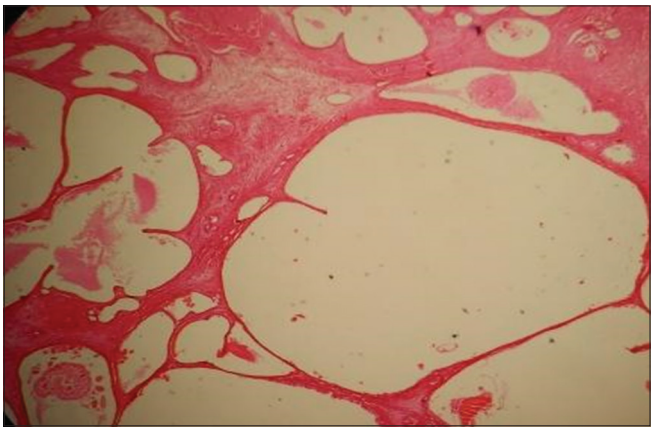

Figure 2: Cystic change in benign hyperplasia prostate (H and E stain, ×100)

Table 1: Distribution of BHP cases according to age groups

Age group (in years)	Number of BHP cases	Percentage
30-39	1	1.17
40-49	1	1.17
50-59	9	10.59
60-69	34	40
70-79	35	41.17
80-89	5	5.90
Total	85	100

BHP: Benign hyperplasia prostate

BHP

Microscopically BHP was seen characterized by the presence of glandular and stromal hyperplasia and the acini being lined by bilayer of cells (Figure 1). Corpora amylacea in acini, cystic changes (Figure 2), squamous metaplasia, transitional cell metaplasia and calcification were among the variably present associated features. Among the 85 BHP cases, the youngest patient was 37 years old and the oldest was 85 years old and the peak incidence was seen in 70-79 years age group. The detailed age distribution is given in Table 1.

On the basis of histological composition five types of BHP growth patterns are described, i.e., fibromyoadenomatous, fibroadenomatous, fibromuscular, muscular and stromal. In fibromyoadenomatous type, hyperplasia of glandular as well as stromal components was seen while only hyperplasia of glandular elements was seen in fibroadenomatous type. Fibromuscular type showed mainly stromal proliferation with very little glandular components. Stromal hyperplasia showed predominantly the presence of loose fibrous tissue having interspersed groups of spindle-shaped cells (Figure 3). Fibromyoadenomatous type was found to be the most common. The detailed distribution of these is given in Table 2.

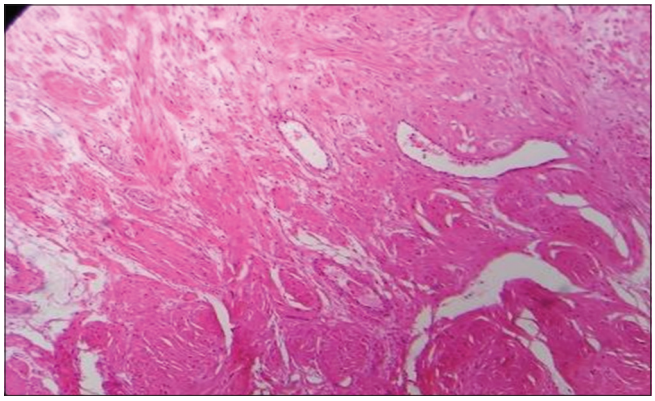

Figure 3: Stromal variant of benign hyperplasia prostate (H and E stain, ×100)

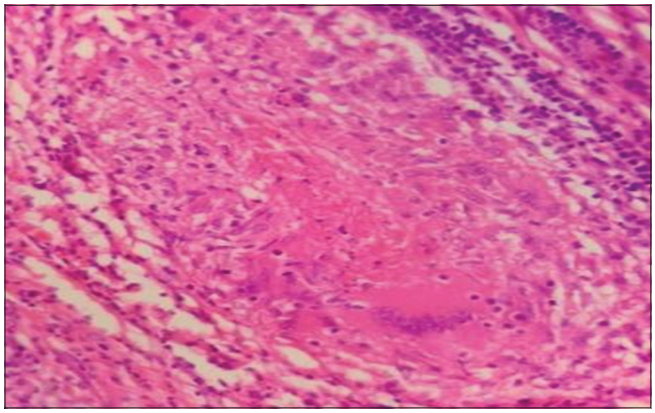

Figure 4: Granulomatous prostatitis (H and E stain, ×400)

Prostatitis

Inflammatory changes affecting prostate were divided, into acute, chronic and granulomatous, on the basis of inflammatory cells present. Prostatitis was seen associated with quite a few cases of BHP. Chronic prostatitis was seen in 32 (34.78%) and acute prostatitis was seen in 6 (6.52%) of prostatic biopsies. 2 (2.17%) cases of granulomatous prostatitis (Figure 4) were also noted. 2 prostatic biopsies were having an admixture of acute and chronic inflammatory cell infiltrations.

Prostatic Adenocarcinomas

In our study of 92 prostatic lesions, 7 cases (7.6%) were diagnosed as prostatic adenocarcinomas and among these cases the youngest patient was 58 years old and the oldest was 82 years old and the peak incidence was seen in 70-79 years age group. The detailed age distribution is given in Table 3.

All these cases were graded according to the Gleasons grading system which presently is the most favored microscopic grading system. Gleasons grading system is based on the extent of glandular differentiation and growth pattern of the tumor as seen in lower magnification, under light microscope. Five different patterns are described by

Table 2: Distribution of various growth patterns of BHP

Pattern of growth	Number of cases	Percentage
Fibromyoadenomatous	58	68.2
Fibroadenomatous	22	25.9
Fibromuscular	4	4.7
Stromal	1	1.2
Muscular	0	0
Total	85	100

BHP: Benign hyperplasia prostate

Table 3: Distribution of prostatic adenocarcinoma according to age groups

Age groups (years)	Number of cases of prostatic adenocarcinoma	Percentage
50-59	1	14.28
60-69	1	14.28
70-79	2	28.58
80-89	3	42.86
Total	7	100

Table 4: Depiction of adenocarcinomas according to Gleasons score

Gleasons score	4	5	6	7	8	9	10	Total
Number of cases	0	1	1	1	2	2	0	7
Percentage	0	14.28	14.28	14.28	28.58	28.58	0	100

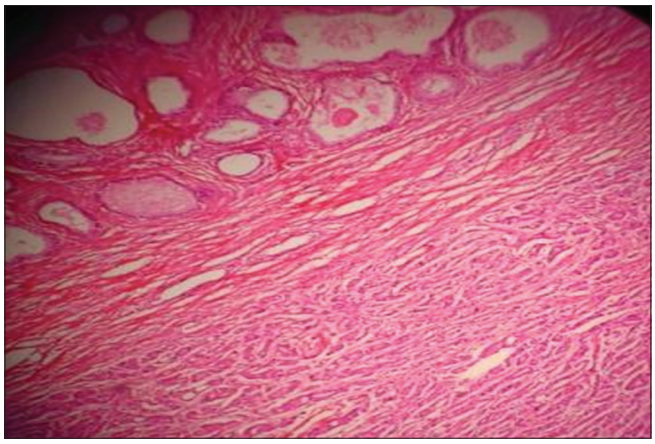

Figure 5: Features of benign hyperplasia prostate and prostatic adenocarcinoma in single focus (H and E stain, ×100)

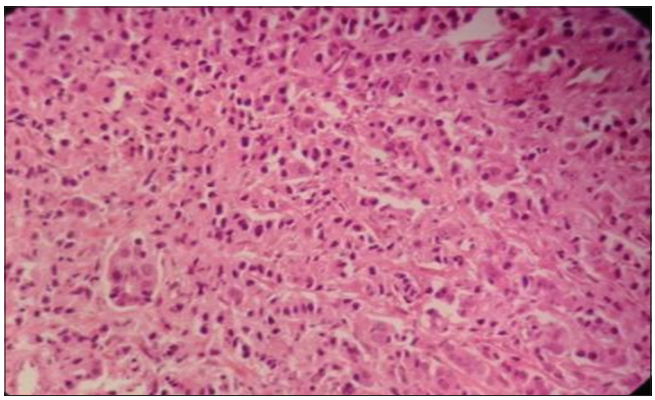

Figure 6: Prostatic adenocarcinoma (H and E stain, ×400)

this system. Both the primary (predominant) and secondary (second most prevalent) architectural patterns are identified and assigned a grade from 1 to 5, with 1 being the most differentiated and 5 being undifferentiated. The combined Gleason grades (Gleason score) range from 2 (1 + 1 = 2), which represents tumors uniformly composed of Gleason pattern 1 tumor, to 10 (5 + 5 = 10), which represents totally undifferentiated tumors. In our study, prostatic adenocarcinoma (Figures 5 and 6) with Gleasons score 8 and 9 were the most common with 2 cases each, and there was no tumor with Gleasons score 2, 3, 4, or 10. Table 4 depicts distribution of various cases of adenocarcinomas with reference to their Gleasons score.

DISCUSSION

Prostatic diseases cause a significant morbidity and mortality in elderly males. The pathological processes affecting the prostate gland with sufficient frequency to merit discussion are BHP, prostatitis and prostatic cancer. Of these three, BHP is the most common seen lesion. In the present study of 92 cases of prostatic lesions, 85 (92.4%) cases were diagnosed as BHP and 7 (7.6%) cases were diagnosed as of prostatic cancer. We observed that 92.3% of all prostatic lesions were of BHP, while 6.3% were of prostatic cancer. These findings are similar to the studies done by Jehoram *et al.*,[8] Bal *et al.*,[9] and Dawam *et al.*[10] whose studies found 93%, 87%, and 86% cases of BHP in their studies, respectively. However, studies by Mansoor[11] from Saudi Arabia showed lesser percentage of BHP cases and more cases of adenocarcinoma as compared to our studies and many Indian studies. In our study, BHP was seen most common affecting age group 70-79 years with 41.17% cases, followed by age group 60-69 years with 40 % cases. This finding is similar to the study done by Deshmukh *et al.*[12] and Shakya *et al.*[13] Both these studies also showed similar results, with nearly 80% of BHP cases affecting these two decades of life. The most common histological pattern of BHP was found out to be fibromyoadenomatous type with 58 (68.2%) cases, followed by fibroadenomatous with 22 (25.9%) cases. Deshmukh *et al.*[13] and Kim and Kim[14] in their studies found similar distribution of various histological patterns of BHP.

Chronic prostatitis was seen in 32 prostatic biopsies, and in the majority of cases was of mild intensity. Acute prostatitis and granulomatous prostatitis were seen in 6 and 2 cases, respectively. All these cases were seen associated either with BHP or prostatic adenocarcinoma. These findings are similar to most of the studies on prostatitis, like the study of Anim *et al.*[15] and Mohammed *et al.*,[16] which also found chronic prostatitis as the most common inflammatory lesion affecting prostate followed by acute and granulomatous prostatitis.

Prostate cancer is one of most common malignancies in the world, particularly significant among elderly males. More than 75% cases of all prostate cancers occur in males more than 60 years age. In our study Prostate cancer was found to be affecting 7 (7.6%) cases of all the 92 cases studied and all these 7 cases were of prostatic adenocarcinoma. These findings were in agreement with the studies of Subathra and Sangeetha,[17] Deshmukh *et al.*[13] and Jatav *et al.*[18] who also found 7.4%, 9% and 9.7% of all prostatic lesions as prostatic adenocarcinoma, respectively. These studies also found adenocarcinoma as the principal variant of prostatic cancer, constituting more than 90% of all prostatic cancer cases. Elem and Patil[19] in their studies found all prostatic malignancies to be of prostatic adenocarcinoma. We found in our study prostatic adenocarcinoma affecting later decades of life, with the youngest patient affected being 52 years of age. Maximum percentage of patients were seen in their 8th and 7th decade of life which was in close concordance with the studies of Gilliland and Key[20] and Matapurkar and Taneja.[21] In our study, we found 4 (56.16%) cases of adenocarcinoma with Gleason score of 8-9. Angurana[22] in her studies found 64.3% cases with

Gleasons score 6-10 which was in close agreement with our study. Whereas doing the Gleasons grading for 71 cases of prostatic adenocarcinomas, Albasri *et al.*[23] found Gleasons score of 5-7 as the commonest followed by Gleason score 8-10. Majority of the cases of prostatic adenocarcinoma were poorly differentiated in our study.

CONCLUSION

We found the pattern of prostatic diseases in Garhwal region, were similar to other regions of India and world. BHP was the most common encountered lesion seen in the prostate and was on many occasions associated with prostatitis. Fibromyoadenomatous pattern was seen to be the most common growth pattern of BHP. Prostatic adenocarcinoma was found in about 7% cases, and the majority of these cases were of high-grade adenocarcinoma and was of Gleasons score 7-9.

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Original Article

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Evaluation of the Effect of Intrathecal Nalbuphine as an Adjuvant to Spinal Bupivacaine for Post-operative Analgesia in Patients Undergoing Abdominal Hysterectomy: A Randomized, Double-Blinded Control Trial

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Abstract

Background: Nalbuphine is a synthetic mixed agonist-antagonist opioid, which produces k receptor mediated analgesia to control mild to moderate pain without producing μ receptor mediated side effects when used intrathecally (IT) with bupivacaine.

Aim: To evaluate the onset, quality and duration of sensory, motor blockade, post-operative analgesia, and it's side effects if any when nalbuphine is added as an adjuvant for spinal anesthesia in the abdominal hysterectomies.

Methodology: 60 patients of ASA Grades I and II in the age group of 30-60 years were randomly allocated to one of the two groups. Group B (*n* = 30) received 0.5% hyperbaric bupivacaine {3cc (15 mg) + 0.5 ml sterile water} IT; Group N (*n* = 30) received 0.5% hyperbaric bupivacaine {3cc (15 mg) + 0.5 ml (1 mg) nalbuphine} IT.

Observations: The characteristics of onset of sensory and motor blockade, duration of effective analgesia (visual analog scale [VAS] score), perioperative hemodynamics, respiratory parameters, and side effects were recorded, tabulated, and statistically analyzed.

Results: The onset of sensory and motor blockade was faster in Group N. The two segment regression time was significantly prolonged in Group N compared to Group B. The total duration of effective analgesia (time from IT drug injection to the point of time when VAS ≥4) was also significantly prolonged in Group N compared to Group B. The hemodynamic, respiratory parameters and intraoperative complications were comparable in both the groups.

Conclusion: IT nalbuphine improved the quality of intraoperative and post-operative analgesia with minimal side effects.

Key words: Nalbuphine, Post-operative analgesia, Spinal anesthesia

INTRODUCTION

Spinal anesthesia is in existence since more than a century, and it is still very common regional anesthesia technique done even today. The local anesthetic drugs used had limited duration of action, hence the need for adjuvants such as opioids, alpha 2 agonists, neostigmine, and magnesium. Among them, the intrathecal (IT) opioid administration has been found to provide superior quality of analgesia after a variety of surgical procedures.

The reason for mixing of opioids and local anesthetics is that this combination will eliminate the pain by acting at two different locations, local anesthetics acting at the nerve axon and the opioids at the receptor site in the spinal cord.

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Nalbuphine is a highly lipid soluble opioid with an agonist action at the kappa and an antagonist activity at the mu opioid receptors. Nalbuphine and other kappa agonists had provided reasonably effective analgesia in some models of visceral nociception. As Nalbuphine is an agonist-antagonist, it is unlikely to cause side effects such as respiratory depression, urinary retention, pruritus, and excessive sedation, due to its action at kappa receptors.

There are very few studies of IT nalbuphine for post-operative analgesia, and because of this reason, we have decided to take up this randomized study to evaluate the effects of IT nalbuphine 1 mg added to 0.5% hyperbaric bupivacaine in patients undergoing an abdominal hysterectomy.

METHODOLOGY

After getting approval from Institutional Ethics Committee and written consent, 60 patients, ASA I and ASA II, in the age range of 30-60 years, posted for abdominal hysterectomy were selected.

Exclusion Criteria

Patients with a respiratory disorder and those with a prior history of opioid and other substance abuse, history of drug allergy, and also those unwilling to participate in the study, ASA Grade III and IV and any contraindication to spinal anesthesia were omitted from the study.

All the selected patients were explained about the assessment of pain with the help of visual analog scale (VAS), and then their written and informed consent was taken.

Patients were randomly allocated into two groups of 30 each. Patients in Group B were given 0.5% bupivacaine heavy (3 cc) + 0.5 ml sterile water while patients in Group N were given 0.5% bupivacaine heavy (3 cc) + 0.5 ml (1 mg) nalbuphine for spinal anesthesia.

Patients were premeditated with injection atropine 0.6 mg I.M and injection Ranitidine 50 mg I.V, both ½ h before surgery. Preloading was done with ringer lactate 10 ml/kg body weight 20 min before spinal anesthesia was given by taking into consideration all aseptic and antiseptic precautions, using 25 g Quincke type spinal needle. Patients were turned supine immediately at the end of the injection and observations were recorded as shown below:

Sensory Block - Assessed by Using "Pin-Prick" Method

1. The onset of sensory block: Immediately after the spinal injection was given, patients were checked for loss of pinprick sensation at L1 dermatome, and that time was taken as an onset of sensory block
2. The highest sensory level achieved
3. Two segment regression time: The time interval from highest sensory level to two segment regression of the sensory block
4. Duration of sensory block: The time interval from the onset of sensory block to regression of sensory level to L1 dermatome again.

Motor Block- Assessed by the Bromage Scale

1. Grade 0 - No muscular weakness
2. Grade I - Unable to flex the hip
3. Grade II - Unable to flex the knee
4. Grade III - Unable to flex the ankle.

Following things were observed in motor block:

1. The onset of motor block: The time interval from IT injection to achievement of motor block of Bromage Grade I
2. Maximum motor block achieved
3. Duration of motor block: The time interval from the onset of motor block to regression of motor block to Bromage Grade 0.

Recordings of pulse rate, blood pressure, SPO2, respiratory rate were done at 1, 3, 5 min and then every 5 min until 15 min and every 15 min until the end of the procedure

Intraoperative sedation scores were defined by Ramsay sedation score. After the operation, pain, sensory level, and motor block were evaluated at every 30 min during the first 2 h, and at every 60 min for the next 6 h, and at 12 and 24 h after arriving in the recovery room. Visual analog scale was used to evaluate the pain intensity. Side effects of pruritus, post-operative nausea and vomiting (PONV), sedation, urinary retention, euphoria or dysphoria, and respiratory depression were recorded for 24 h. The durations of complete analgesia (time from the IT injection to the first pain report, VAS score >1) and effective analgesia (time from the IT injection to the first analgesic requirement, VAS score >3) were noted. At this time, patients were given rescue analgesic- injection diclofenac sodium 1.5 mg/kg. Intramuscular Patients were monitored for various intra and post-operative complications. All the recorded data were statistically analyzed, and the significance was measured as a probability of occurrence by the *t*-test.

1. $P > 0.05$ - Not significant
2. $P < 0.05$ - Significant
3. $P < 0.001$ - Highly significant.

RESULTS

The two groups are nearly similar to each other demographically in age, weight, and ASA physical status.

No major difference was found in various hemodynamic or vital parameters between the two groups. However, there was a significant difference in $P<0.001$ between mean onset and a complete sensory block in Group N and Group B. The mean onset and complete motor block in Group N and Group B also showed statistical significance in $P<0.05$. Group N has shown a faster onset compared to Group B in both the cases. The distribution of sensory level in both the groups was similar; the maximum was reached up to T8 level. The mean regression in sensory (taken as regression up to L1 level) and motor block in Group N and Group B showed statistical significance ($P < 0.001$). Similarly, mean duration of requirement of first rescue analgesia in Group N and Group B showed significant difference in $P < 0.001$, this has highlighted the fact that Group N had prolonged post-operative analgesia. Group N showed a significantly higher median Ramsay sedation score than Group B, $P < 0.001$ (Table 1).

There was a drop in the systolic blood pressure, but it was not statistically significant. There was no change in the mean respiratory rate as well as mean oxygen saturation as measured by pulse oximeter during intra, as well as post-operative periods ($P > 0.05$). Side effects, such as nausea, vomiting, and urinary retention, were observed in Group N in one patient each. In Group B, two patients had nausea, and another two had urinary retention.

DISCUSSION

Spinal anesthesia is the preferred technique for gynecological surgeries. Pain and stress-free post-operative period bring about early mobilization and recovery thereby reducing the morbidity and mortality of any surgical operation. It has been well-documented that the combination of opioid and local anesthetics administered IT has a synergistic analgesic effect thus providing powerful potentiation of analgesia by local anesthetic. Opioids, however, act through various receptors.[1,2] Spinal opioids can provide profound post-operative analgesia with fewer central and systemic adverse effects than with opioids administered systemically.[3] Most commonly used IT opioids are mu agonist drugs that provide excellent analgesia but carry along with them various mu- mediated side effects.[4] Eventually, it was established that significant analgesia can be obtained by kappa binding sites as well with the added advantage of bypassing mu related side effects.[2,4]

Table 1: Onset, duration of sensory, motor block, and first rescue analgesia (mean±SD)

Parameter	Group N	Group B	*P* value
Onset of sensory block (min)	1.63±0.57	3.23±1.03	<0.001
Onset of motor block (min)	3.77±1.21	4.87±1.76	<0.003
Two segment regression time	99.6±9.86	72.33±9.35	<0.001
Duration of sensory block (min)	362.50±34.71	133.33±25.53	<0.001
Duration of effective analgesia	420.4±25.30	170.83±27.59	<0.001
Median Ramsay sedation score	3	2	<0.001

SD: Standard deviation

Nalbuphine is a mixed agonist-antagonist drug, when it binds to kappa receptor, has the agonistic activating effect similar to that of endogenous dynorphins,[4] and it competitively displaces other mu agonists from the mu receptor, thereby exhibiting less respiratory depression.

In the present study, bupivacaine with nalbuphine as an adjuvant to see the duration of analgesia after the operation and side effects was used. After the subarachnoid block was given, there was a significant difference between the onset of sensory and motor block in Group N.

Our results have shown that the onset of sensory and motor block was faster and time taken to attain complete sensory and motor block to occur was shorter in the N Group as compared to B Group. The mean onset of sensory block in Group N was 1.63 ± 0.57 min compared to 3.23 ± 1.03 min in Group B. The $P < 0.001$ is statistically significant (Graphs 1 and 2).

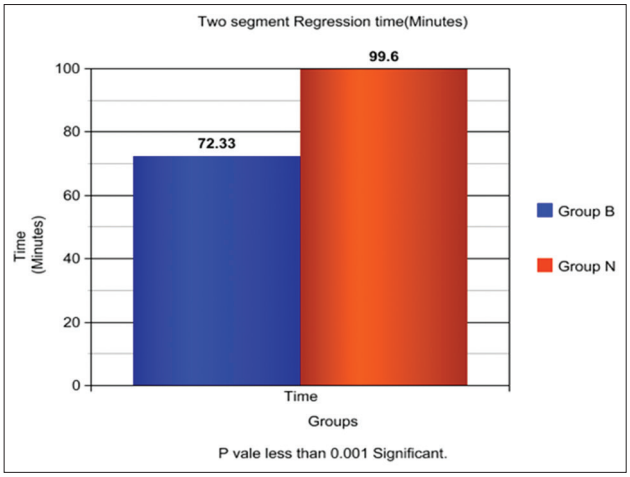
The same type of results were documented by Xavier *et al.*,[5] in their study of 100 female patients posted for elective cesarean section who were given three different doses of nalbuphine (0.2 mg, 0.8 mg, or 1.6 mg) or morphine (0.2 mg) IT. They found that IT nalbuphine provided significantly faster onset of pain relief compared to IT morphine, probably due to its lipophilic nature. Xavier *et al.*, in 2000, performed a comparative study to evaluate post-operative analgesia and adverse effects after using three doses, i.e., 0.2 mg, 0.8 mg, and 1.6 mg of IT nalbuphine or morphine 0.2 mg given for cesarean section along with bupivacaine. The longest durations of complete and effective analgesia among the nalbuphine-treated groups are provided by 0.8 mg added to bupivacaine. Neither pruritis nor PONV was observed with nalbuphine 0.2 and 0.8 mg. IT nalbuphine 0.8-1.6 mg improved the quality of intraoperative analgesia and provided a significantly faster onset of pain relief, compared with IT morphine, probably due to its lipophilic properties. They concluded that 0.8 mg of IT Nalbuphine improves intraoperative analgesia and delays early post-operative analgesia without increasing the risk of any side effects.

In contrast to these studies, Tiwari *et al.*,[6] in their study, have shown that onset of sensory and motor blockade was not affected by adding nalbuphine IT. In a study of 75 patients posted for lower limb and lower abdominal surgeries, who received either 0.2 mg or 0.4 mg nalbuphine or plain bupivacaine IT. This disparity in the onset of the

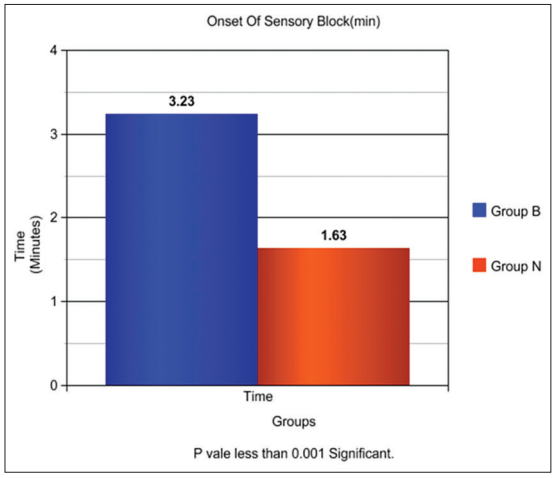
blockade could be related to the lower dose of nalbuphine used in this study.[6] The effect of addition of nalbuphine to bupivacaine used for elderly patients undergoing surgeries under spinal anesthesia and in patients scheduled for lower abdominal and the lower extremity surgeries concluded that nalbuphine provided post-operative analgesia for 8-9 h without any adverse side effects.[7]

We observed that the post-operative regression of sensory and motor block was significantly delayed in Group N than in Group B, (Graphs 3 and 4) and the first rescue analgesic requirement in Group N (420.4 ± 25.3 min) was significantly delayed than in Group B (170.83 ± 27.59 min). (Graph 5) These results are in accordance with the study done by Mukherjee *et al.* He demonstrated that the longest duration of post-operative analgesia was the group in which 0.8 mg nalbuphine was used as an adjuvant as compared to lower doses of nalbuphine, i.e., 0.2 and 0.4 mg.

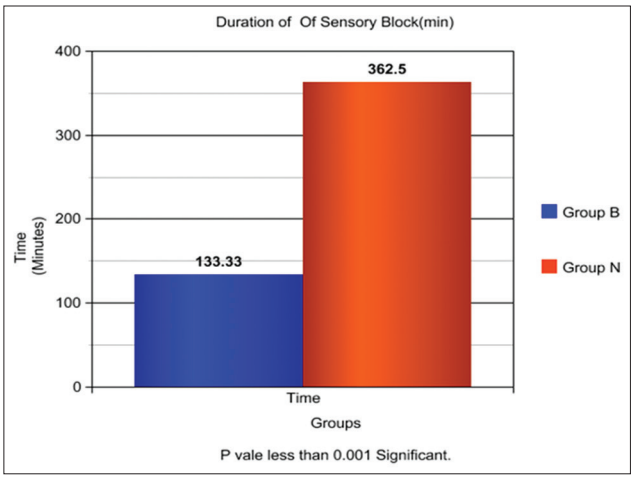
In the year 2011, Mukherjee *et al.*,[8] formulated a study to determine whether nalbuphine prolongs analgesia by comparing with control and to find out the optimum dose of IT nalbuphine by comparing the 0.2, 0.4, and 0.8 mg doses which prolonged post-operative analgesia without increased side effects. It was observed that effective analgesia increased with increase in concentration, and the



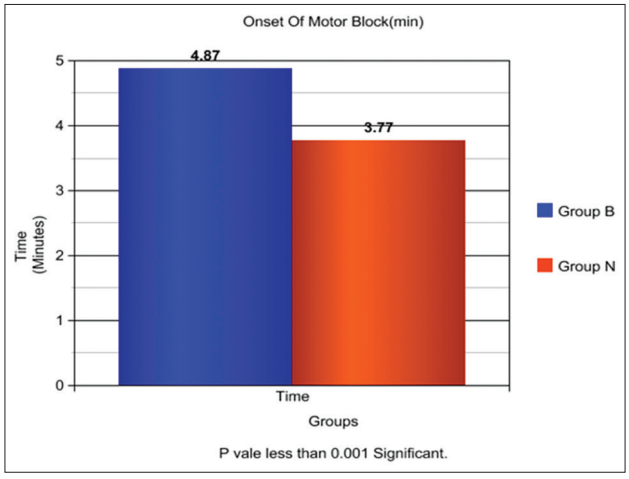
Graph 3: Two segment regression time (min)



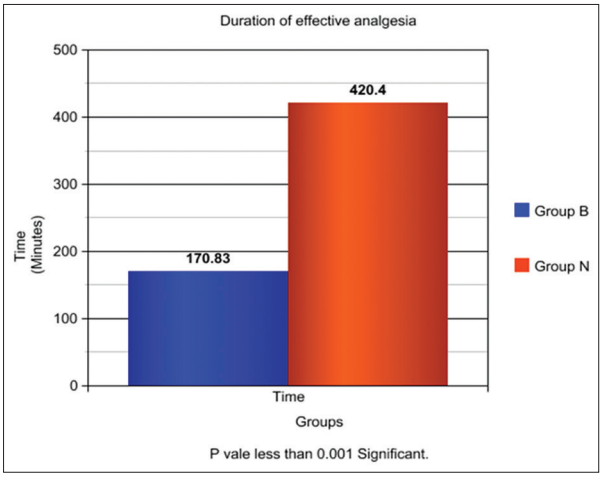
Graph 1: Onset of sensory block (min)



Graph 4: Duration of sensory block (min)



Graph 2: Onset of motor block (min)



Graph 5: Duration of effective analgesia

final observation of prolongation of analgesia was with 0.4 mg of nalbuphine with 0.5% hyperbaric bupivacaine without any side effects.

A study by Gear *et al.*,[9] suggests that women report higher pain levels or exhibit less tolerance than men for a given stimulus intensities and Kappa opioid analgesia is greater in females than males, that proves that Kappa agonist drugs like nalbuphine can be used to control the visceral pain caused by hysterectomy.

During spinal anesthesia, as the patient is conscious about the surroundings, most of the time it becomes necessary to sedate the patient as this will reduce his anxiety and also minimizes the awareness about routine operating room proceedings. IT nalbuphine has an added advantage of providing intraoperative sedation thus reducing or even abolishing the need for any other sedative drug.

In our study, Group N, 23 out of the 30 patients, had an intraoperative Ramsay sedation score of 3 or 4 as compared to only 3 patients in Group B. Xavier *et al.*, found comparable sedation scores in all four groups in their study, because of the fact that they were comparing sedation scores of nalbuphine with morphine, and morphine in itself has some sedative effects.[7]

Opioid receptor activation reduces intracellular cyclic adenosine monophosphate formation and opens the potassium channels (mu and delta) or suppresses voltage-gated N-type calcium channels (Kappa receptors). These actions result in neuronal hyperpolarization and reduced availability of intracellular calcium that will lower neurotransmitter release by central nervous system and myenteric neurons,[10] thereby prolonging the duration of effective analgesia.

In the year 2011, Mostafa *et al.*,[11] compared the analgesic effects and duration of analgesia as well as the side effects of 50 mg tramadol or 2 mg nalbuphine, which was administered *via* the IT route for post-operative pain relief after transurethral resection tumor of the bladder. They concluded that in both the groups there was similar motor block, nearly equal analgesia, delayed first analgesic request, and less analgesic supplement over the first 24 h of operation. No significant post-operative complications, such as itching, respiratory depression, neurological sequelae, were observed among the two groups.

The practice of administering IT nalbuphine for more than ten years did not have any reports of neurotoxicity. The previous studies have been conducted on pregnant patients also but did not reveal any untoward effects.

In the year 1991, Rawal *et al.*,[12] has studied the behavioral and histopathological effects following IT administration of butorphanol, sufentanil, and nalbuphine in sheep. They concluded that nalbuphine was the least irritating to neural tissue even when it was used in large doses, and it was associated with minor behavioral and electroencephalogram changes.

On statistical analysis, patients belonging to Group B complained of pain earlier than that of Group N. Patients who received bupivacaine with nalbuphine had significantly longer duration of the first request for analgesia when compared to patients who received bupivacaine alone ($P < 0.001$), and this is highly significant. On inter and intra group comparison, there were no significant changes in pulse rate at any time during the intraoperative period. However, the fall in blood pressure did occur but it was not of the grade of hypotension, i.e., change in blood pressure of <20% of baseline value and hence, this falling blood pressure is considered as physiological fluctuations only.[13] Intergroup comparison showed no statistically significant value. In our study, there was no significant change in respiratory rate during the intraoperative and post-operative period in both the groups. Nalbuphine exhibits ceiling effect for respiratory depression.[14,15] Since respiratory depression is predominantly μ receptor-mediated effect and nalbuphine is a μ receptor antagonist, respiratory depression effect is expected to be attenuated by nalbuphine. None of the patients had other μ related side effects such as urinary retention, constipation, and pruritis.

CONCLUSION

In conclusion, addition of nalbuphine in the dose of 1mg to IT hyperbaric bupivacaine 0.5%, in patients undergoing abdominal hysterectomy hastens the onset of both the sensory and motor block, prolongs the two segment regression time, duration of sensory block, duration for first rescue analgesic, provides desirable sedation intraoperatively along with maintaining stable hemodynamic, and respiratory parameters without any significant perioperative complications.[16]

We conclude that nalbuphine can be used as an effective adjuvant along with IT hyperbaric bupivacaine to provide a pain-free post-operative interval.

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Original Article

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Role of Conservative Management of Traumatic Chest Injuries: A Retrospective Study & Review of Literature

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Abstract

Introduction: Chest injuries continue to be a major cause of acute respiratory distress with its morbidity and mortality in otherwise healthy young people. Airway access and control, oxygen therapy, and chest tube drainage are the mainstay of therapy. Chest tube drainage carries a risk of complications ranging from minor in over one-third of cases to around a 5% incidence of more serious events.

Objectives: To examine the management of traumatic chest injuries in surgery department where some of these injuries do not receive chest tubes.

Materials and Methods: A retrospective study of the management of traumatic hemo/pneumothorax performed in surgery department where many of these injuries have been treated conservatively.

Results: 60 patients with chest injuries in a year identified. Of these, 35 patients (58.3%) were initially managed without chest tube. 3 patients subsequently required chest tube insertion due to radiological enlargement of the pneumothorax. No patients worsened during conservative treatment.

Conclusion: Chest tube insertion for mild or small sized traumatic chest injury may be avoided, if there are no associated significant injuries.

Key words: Chest injuries, Chest tube, Conservative, Hemothorax, Pneumothorax, Trauma

INTRODUCTION

Chest injuries secondary to trauma are on the rise due to increased frequency of road traffic accidents (RTAs) and increase in community violence. RTAs stand first among all traumatic injuries and are in the rising trend in India even in rural population.[1] The number of accidental deaths in India is more when compared to the Western World.[1] Thoracic trauma contributes heavily to these figures along with head injury, orthopedic injuries, and abdominal injury. Approximately, one-quarter of civilian trauma deaths are caused by trauma to thorax, and many of these deaths can be avoided by precise diagnosis and proper management.[2]

Managing a grievously injured patient presents a clinical challenge, especially in semi-urban and rural centers. The combination of clinical foreknowledge, ability to spot changing clinical signs, and even-tempered surgical courage to perform simple but lifesaving procedures can bring about a profound difference in outcome for the chest injured patient - even in resource-limited settings.[3]

In spite of all these, chest tube insertion for traumatic chest injuries can lead to significant morbidity and complications. In 1997, Collop *et al.* reported 3% early complication rate including misplacement and an 8% delayed complication rate including dislodgement, infection, and kinking.[4]

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Chest tubes are a source of intrathoracic infections such as empyema and pneumonia. However, the efficacy of antibiotics given as prophylaxis against such complications has not been substantiated.[5,6] Nevertheless, there have been some more serious misplacements, for example, perforation of the left atrium[7] and liver injury with a large bore chest tube[8] and vascular injuries, esophageal injuries, chylothorax, and cardiac dysrhythmias.[9]

Some of the chest injuries leading to hemothorax and pneumothorax can be managed conservatively without chest tube drainage provided it is mild or small, and the patient is able to maintain oxygenation without supportive treatment.

In this study, we examine the management of traumatic pneumo/hemothorax in our department where some of these injuries are managed without chest tube drainage.

MATERIALS AND METHODS

Patients treated at the Department of General Surgery at R. L. Jalappa Hospital, Tamaka, Kolar, India with a diagnosis of traumatic chest injury were identified by a search of the departments' computerized database from the period of 1st January 2014 to 31st December 2014. The hospital notes and A and E records were retrieved, and information obtained concerning the cause, nature, and mode of injury, the presence of other associated injuries, and the method adopted for the treatment of traumatic chest injury. Associated injuries which needed some surgical procedure for the patient were defined as significant. As the radiographic technique was variable, the effort to quantify the size of the pneumo/hemothorax was limited. The records containing the clinical assessment of the patient, treatment, and outcome were analyzed.

RESULTS

The retrospective study included a total of 60 patients, of which 49 (81.6%) were male patients, and 11 (18.3%) were female patients (Table 1). In this study, chest injury was highest in the 3rd decade of life, accounting 45% of cases. The lowest incidence observed in 10-20 years age group, i.e., 3% of cases. Mean age was 39 years (Graph 1).

The mechanisms of injury and methods of treatment shown in Tables 2 and 3).

Initial treatment involved insertion of a chest tube in 25 patients with a chest injury. The majority of patients, in this group, had significant associated injuries. Most of these patients were from RTAs.

Table 1: Distribution of patients according to gender in the study

Sex	Number of patients (%)
Male	49 (81.6)
Female	11 (18.3)
Total	60 (100)

Table 2: Distribution of patients according to mode of chest injury in the study

Cause	Number of patients	Percentage
RTA	40	66.6
Assault	6 (1 knife stab)	10
Fall from height	10	16.6
Building	(4)	
Tree	(6)	
Self-fall	2	3
Fall of heavy object	1	1.6
Others	1 (bull gore injury)	1.6
Total	60	100

RTA: Road traffic accidents

Table 3: Number of pneumo/hemothorax by mechanism of injury, and mode of management

Mechanism of injury	Conservative management	ICD insertion	Total
RTA	21	19	40
Falls	5	5	10
Assault	3	3	6
Industrial	1	0	1
Other significant injuries	2	1	3
Total	32	28	60

RTA: Road traffic accidents

In 35 chest injury patients, initial management was observation only, either as an inpatient or as an outpatient. Chest tube insertion subsequently undertaken in 3 patients because of radiological enlargement of the pneumothorax 4 h after admission. None of these patients had clinical deterioration before insertion of the chest tube. A total of 32 patients were managed conservatively and recovered without a chest tube.

All patients with hemo/pneumothorax treated conservatively were described as "mild" or "small." All chest injuries described as "large" or "severe," were treated initially with chest tube insertion.

The retrospective study included total of 60 patients of which 81.6% were male, and only 15.3% were female patients.

In our study, 3rd decade of life shows the highest incidence of chest injuries, accounting to 45%. The lowest incidence was observed in 10-20 age group, i.e. only 3%. Mean age was 39 years (Graph 1).

RTA being the most common mode of injury in our study accounting as high as 66.6% of the total 60 patients. There were 10% patients with chest injuries because of assault, of this only one had assault with a knife. 16.6% of patients sustained chest injuries due to fall from height. (Table 2)

Most of the patients had multiple complaints on presentation, of which most common was chest pain (36 patients) followed by an external wound (32 patients). Least common presentation was unconsciousness, which was seen in only 3 patients (Graph 2).

In our study, among 60 patients, 42 patients had a pneumothorax, 12 patients had hemothorax, 5 patients had hemo/pneumothorax, and only 1 patient had tension pneumothorax (Graph 3).

In our study, most common clinical sign noticed was positive chest compression seen in 65.3% patients, followed by reduced breath sounds in 38.4% patients. Tracheal deviation and paradoxical breathing were the least common signs and were noted in one patient each (Graph 4).

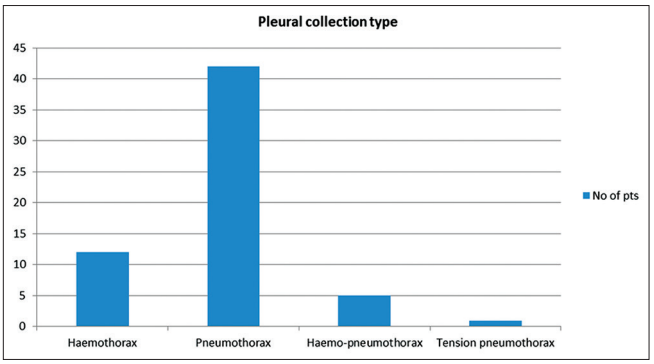
Among 60 patients, 32 patients were managed conservatively and 28 patients with chest tube insertion (Pie chart 1).

DISCUSSION

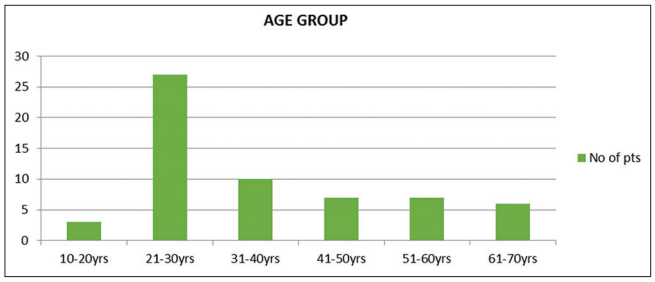
Chest injuries, often a part of polytrauma, were isolated injuries in this study. The majority of the patients were managed conservatively without the insertion of a chest tube. This suggests that some traumatic pneumo/hemothorax will resolve spontaneously when managed conservatively.

Catheter aspiration for simple pneumothorax for outpatient management has been reported.[10] However, conservative management of chest injuries is rarely followed.

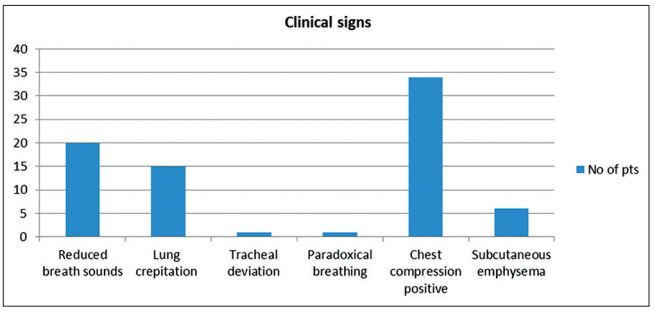
In a large South African series of predominantly penetrating injuries to the chest,[11] traumatic pneumothorax were initially managed conservatively if there was <20% reduction in lung volume. More than 40% patients were initially managed conservatively. In 10% of these, a chest drain insertion was subsequently done because of expansion of the pneumothorax.



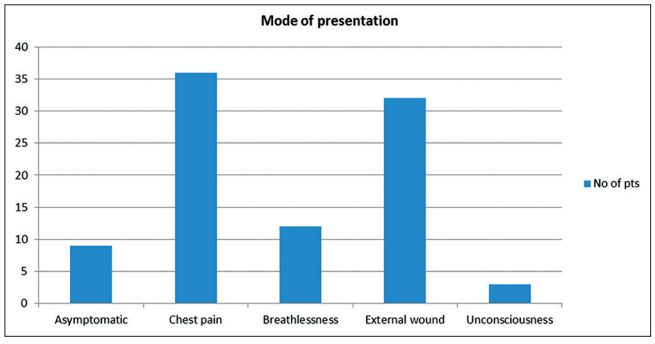
Graph 3: Distribution of patients according to the type of pleural collection in the study



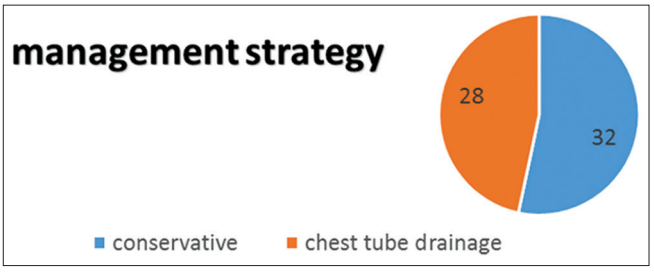
Graph 1: Distribution of patients according to age group



Graph 4: Distribution of patients according to clinical signs in the study



Graph 2: Distribution of patients according to mode of presentation of patients in the emergency department



Pie chart 1: Distribution of patients according to management strategy of patients in the study

Occult pneumothorax, defined as those recognized by abdominal computerized tomographic (CT) scanning but not detected on routine screening chest X-rays, occur in 2-6% of patients undergoing CT scanning for blunt abdominal trauma.[12] These patients do not require any further assessment like a repeat chest X-ray. They can be managed conservatively.

There are a few prospective studies which compare the conservative approach with chest tube approach in patients with traumatic chest injuries. One randomized study shows that patients can be treated conservatively in the absence of the use of intermittent positive pressure ventilation (IPPV). However, patients with an occult pneumothorax who also received IPPV had a high rate of progression of the size of their pneumothorax, with 3 out of 21 developing tension pneumothorax.[13]

This approach of conservative management can be applied to patients with mild or small injuries, patients who have no other significant injuries, and patients who are maintaining vital signs and oxygenation. The insertion of a chest tube is therefore not an essential part of the treatment of all chest injuries.[14]

Patients need admission for observation, require pain medication, and monitoring of vital signs. If they develop any signs of respiratory distress, they need to undergo the insertion of the chest tube.

A repeat chest X-ray has to be done after 4 h to see any enlargement of hemo/pneumothorax. Any expansion in the size of hemo/pneumothorax mandates the insertion of the chest tube. Most of the patients with mild or small injuries will resolve spontaneously without exposing the patient to the risks associated with the chest tube insertion.

However, a chest tube is compulsory for patients in respiratory distress on presentation, patients who require IPPV, patients with associated significant injuries, and patients who develop respiratory distress during conservative management.

CONCLUSION

Mild or small sized chest injuries can be managed conservatively without the need for a chest tube. Chest tube insertion is required in patients who present with respiratory distress, need IPPV and patients with associated significant injuries.

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Original Article

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Analysis of Coronary Artery Ectasia: Experience from a Tertiary Care Hospital in South India

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Abstract

Background: Coronary artery ectasias (CAE) could have a prediction for coronary artery disease (CAD). Ectatic coronary arteries even without the presence of coronary stenoses are subject to thrombus formation, vasospasm, and spontaneous dissection. The presence of ectatic segments produces sluggish blood flow, with exercise-induced angina and myocardial infarction, regardless of the severity of coexisting stenotic coronary disease.

Objectives: The present study was done to analyze the incidence of CAE and to check the association of CAE with CAD.

Methods: This was a retrospective study of 7148 patients who had coronary angiogram from 2010 to 2015. Details of the patients and clinical symptoms were analyzed. Electrocardiography was evaluated for various abnormalities. The treadmill test was performed utilizing modified Bruce protocol. The angiogram films were reviewed with two blinded observers.

Results: 257 patients had angiographic evidence of CAE. The most commonly affected vessel was the right coronary artery (88.73%) followed by a left anterior descending artery (41.63%), left circumflex artery (28.79%), and left main coronary artery (5.45%). The most common type of ectasia seen was Type IV ectasia (80%) followed by Type III (9%) and Type II (8%). Lowest percentage distribution (3%) was seen among Type I group. The greater incidence of ectasia was seen in the proximal segment of the coronary arteries compared to the distal segment.

Conclusion: Coronary ectasia can cause flow limiting obstructive lesions and could have guarded prognosis in view of its propensity of layered thrombus formation.

Key words: Coronary angiogram, Coronary artery disease, Coronary ectasia, Right coronary artery

INTRODUCTION

Coronary artery ectasia (CAE) has been recognized as an uncommon pathological finding for many years. The first autopsy-proven demonstration of CAE was done by Morgagni[1] in 1761 and Gougon in 1812. It affects 0.46-4% of general population, but the etiology of the disorder remains uncertain. CAE or aneurysmal coronary artery disease (CAD) is defined as dilatation of an arterial segment to a diameter of at least 1.5 times that of the adjacent normal coronary artery. CAE can be found in up to 5% of angiographic and in 0.22% to 1.4% of autopsy series. It can be either diffuse affecting the entire length of a coronary artery or localized. When the dilatation involves the entire vessel, the word "ectasia" is used instead of an aneurysm. CAE or the aneurysm is attributed to atherosclerosis in 50% of cases, whereas 20-30% have been considered to be congenital in origin. In the great majority of these patients, ectasia coexists with CAD. Only 10-20% of cases of CAE have been described in association with inflammatory or connective tissue diseases. In the western population, the most common association had been with coronary atherosclerosis. Other conditions in which CAE or an aneurysm has been noted include Ehlers Danlos syndrome, polyarteritis nodosa, scleroderma, cystic medionecrosis, trauma, mycotic embolus, syphilitic aortitis, antineutrophil cytoplasmic antibody-related vasculitis, Kawasaki disease, and iatrogenic (angioplasty and atherectomy).[2-6]

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Most published series suggest that the incidence in patients investigated for ischemic heart disease is between 1% and 2.5%. The clinical significance of CAE is not clear. It has been suggested that coronary ectasia alone is as important as the presence of coronary stenosis. Various other studies have shared no difference from a control population with ischemic heart disease. An association with the aortic aneurysm has also been reported, although many series do not mention any relation between the two. It has been stated that the presence of ectasia does not affect the outcome of coronary artery bypass graft unless the graft is sutured to the wall of the ectatic segment. In a study in British Heart Journal, Hartnell[7] reviewed 4993 patients, out of which 70 patients had CAE. It has been suggested that CAE alone may be a cause of angina. In his study, he observed that in patients with angina, ectasia accompanies at least some degree of coronary artery narrowing. Slow or turbulent blood flow in a dilated vessel might be expected to lead to thromboses and a high mortality rate. In the European coronary surgery study, the mortality of those with CAE who were treated medically is similar to the 5 years morality (13% as compared to 10%).

The incidence of CAE is predominantly in men. The right coronary artery (RCA) is more commonly affected followed by left anterior descending (LAD) artery, left circumflex (LCX) artery, and left main coronary artery (LMCA). The presence of ectatic segments produces sluggish blood flow, with exercise-induced angina and myocardial infarction, regardless of the severity of coexisting stenotic coronary disease.[8,9] The introduction of new non-invasive modalities,[10] such as coronary artery computed tomography and magnetic resonance angiography, and the systematic testing of modern antiplatelet and vasoactive medication, look promising for the better treatment and prognosis of these patients.

Clinical literature suggests that ectatic coronary arteries even without the presence of coronary stenosis are subject to thrombus formation, vasospasm, and spontaneous dissection. Newer subgroups of ectasia are increasing with the use of multiple intervention devices to dilate coronary artery stenosis. By design, these destroy the media of the coronary arteries and it is not clear whether these iatrogenic ectatic coronary arteries are subject to the same complication as idiopathic CAE.

The present study was done to analyze the incidence of CAE and to check the association of CAE with CAD. It was also aimed at observing the distribution of CAE with regard to vessel involvement and pattern and to compare the angiographic profile of patients with CAE and CAD.

MATERIALS AND METHODS

This was a retrospective study of 7148 patients who had coronary angiogram from 2010 to 2015 in Sri Ramachandra Hospital, of which 257 patients had angiographic evidence of CAE. The study comprised integrated information in two areas of interest. Details of the patients, mode of presentation- whether atypical chest pain, angina on effort, acute coronary syndrome or acute myocardial infarction alone, with risk factor stratification, such as presence or absence of smoking, hypertension, diabetes mellitus, were noted. A basic investigation like electrocardiography (ECG) was evaluated as to whether it was normal or abnormal as characterized by >1.5 mm depression in ST segment in >2 contiguous leads, >1 mm ST elevation in >2 contiguous leads, abnormal Q waves, R wave progression, conduction defects. 65 patients could not perform stress test either due to the acute presentation of chest pain or a baseline abnormal ECG. The Treadmill test was performed utilizing Bruce protocol in the remaining patients.

The angiogram films were reviewed on a SIEMENS AXIOM ARTIF dFC system with two blinded observers. CAE was defined as at least one localized dilatation of a coronary artery segment to >1.5 times the diameter of the adjacent normal vessel. The incidence of CAE during the study period was noted, and the distribution of ectasia in various coronary arteries and the type of CAE based on Markis classification was also studied. The presence or absence of stenoses and, its severity was noted.

Statistical analysis for comparison of the various data was carried out by the distributive statistics.

RESULTS

257 patients had coronary ectasia, 224 males and 33 females. 105 patients had a history of smoking; 162 had hypertension, and 179 patients had diabetes mellitus. 209 patients had pure ectasia while 48 had an association with CAD.

Graph 1 represents the split up of Type I, Type II, Type III, and Type IV. Type I represents diffuse ectasia of 2 or 3 vessels, Type II represents diffuse ectasia in one vessel and localized disease in another vessel, Type III represents diffuse ectasia of one vessel only, and Type IV represents localized or segmental ectasia. A higher percentage (80%) was seen in Type IV group followed by Type III (9%) and Type II (8%). Lowest percentage distribution (3%) was seen among Type I group.

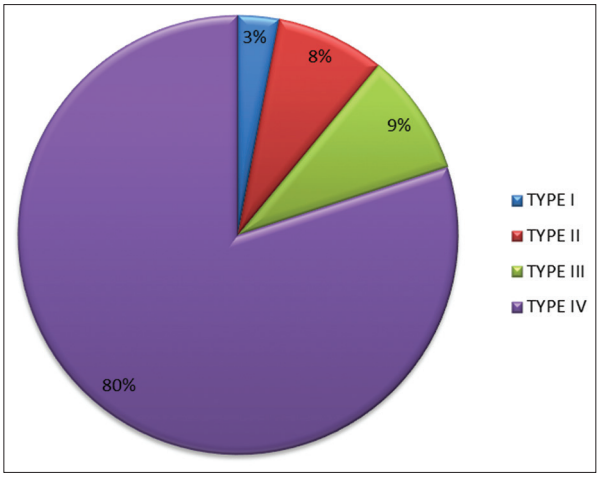
Graph 2 depicts the distribution of ectasia in coronary arteries. The majority (88.72%) were seen among RCA followed by 41.63% in LAD, 28.79% in LCX, and 5.45% in LMCA. The lowest percentage (1.17%) was seen in Ramus intermedius (RI).

Distribution of ectasia and ectasia with CAD are shown in Graphs 3 and 4. Ectasia in proximal LAD is found to be high (33.85%) when compared to ectatic CAD (6.61%), followed by 7.78% of ectasia in LMCA, 5.45% in mid LAD, 4.28% in distal LAD, and the least ectasia (1.17%) was seen in RI. Ectatic CAD in proximal RCA was also found to be high (76.26%), 24.9% had ectasia in mid RCA, 19.46% in proximal LCX, 12.84% in distal RCA, 9.73% in mid LCX, and the least ectasia (4.67%) was seen in distal LCX.

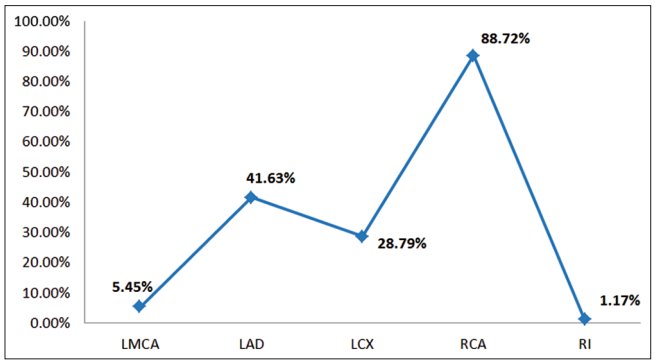
DISCUSSION

In world literature, the incidence of CAE varies from 0.2% to 4.9%.[11,12] In our study, the incidence of CAE is 4% (95% CI 3.2-4.1). The gender difference in incidence has been reported before and has been partially attributed to the lower incidence of CAD in women. In our study, the majority of the patients were males with a mean age of 57.20 ± 10.66 and female had a mean age of 60.09 ± 10.84. This data is in agreement with current literature. There were no cases of the abdominal aneurysm, Marfan's syndrome or connective tissue disorder in our series, and the most common associated disorder was atherosclerotic CAD. The resting ECG was abnormal in the majority of cases, which confirms the findings of Markis *et al.*[13] There was evidence of exercise-induced ischemia in ectasia only group. This suggests that despite the absence of flow-limiting obstruction, ischemia is still manifested as demonstrated by abnormal ECG, typical symptoms or evidence of exercise-induced ischemia. It is likely that endothelial dysfunction abnormalities are involved in the genesis of ischemia in CAE. This is in agreement with current world literature on the significance of CAE. Initially, it was thought of as benign disorder related to connective tissue disorders. However, over the years with the increase in the number of catheterization procedures, availability of procedures to analyze coronary blood flow and quantity perfusion, it is felt that CAE is not benign, is a variant of atherosclerotic CAD and can induce ischemia and infarction in the absence of the significant flow-limiting stenotic CAD.

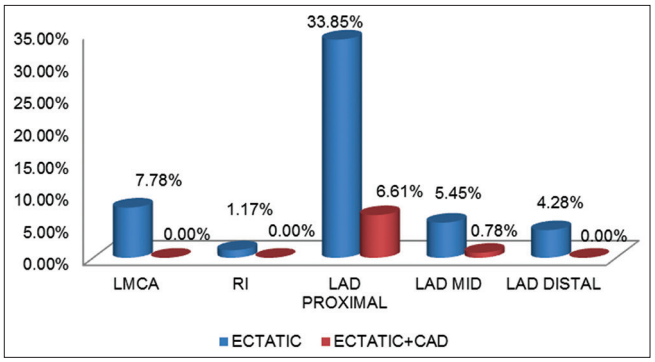
Our angiographic findings were similar to previous reports where the RCA is most commonly affected vessel while the left main, and RI are the least commonly affected. In this series, the most commonly affected vessel



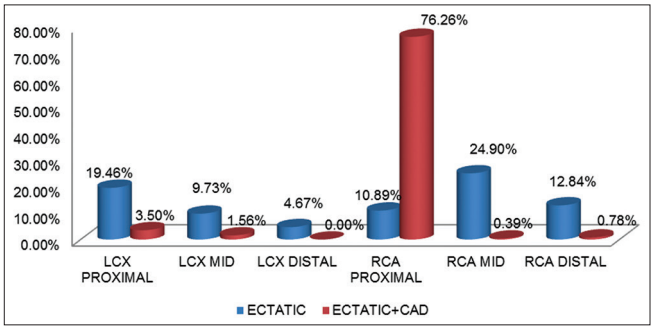
Graph 1: Type of ectasia



Graph 2: Coronary distribution of ectasia



Graph 3: Distribution of ectasia in Left coronary artery



Graph 4: Distribution of ectasia in RCA and LCX

was the RCA (88.73%) followed by LAD artery (41.63%), LCX artery (28.79%), and LMCA (5.45%), RI (1.17%) which is in agreement with data from world literature except a significant increase in the percentage of LAD artery. The most common type of ectasia seen in this series was 80% in Type IV group followed by Type III (9%) and Type II (8%). Lowest percentage distribution (3%) was seen among Type I group. In a study by Valente *et al.*,[14] Type III was more common followed by Type IV and Type I with RCA most commonly affected. Lam and Ho[15] showed that RCA ectasia was more common followed by LAD and the least common involvement with the left main branch.

The greater incidence of ectasia was seen in the proximal segment of the coronary arteries compared to the distal segment. Harikrishnan *et al.*,[16] in his study, also noted a greater incidence of proximal lesions. Diffuse coronary atherosclerosis seems to be most common etiology in this series. An interesting observation was made in this study with regard to co-existent CAD. Only patients who had RCA ectasia had a higher percentage of CAD. In studies by Valente *et al.* and Lam and Ho, the incidence of co-existent CAD was 58.1% and 82%, respectively.

CONCLUSION

The study revealed a 4% incidence of CAE. The management of coronary ectasia is controversial because of bad long term results. Flow limiting obstructive lesions with ectatic arteries also show guarded prognosis in view of its propensity of layered thrombus formation.

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Original Article

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Community-Acquired Urinary Tract Infection: A Study on Responsible Bacteria with their Antibiotic Susceptibility Pattern in Kolkata, India

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Abstract

Introduction: Community-acquired urinary tract infection (CAUTI) is considered to be a common cause for seeking medical care. Since there is a common practice to treat CAUTI empirically before the availability of urine culture sensitivity report, it requires knowledge on the prevailing antibiotic sensitivity pattern of the uropathogens in that region.

Objective: The present study was conducted to determine the distribution and antimicrobial sensitivity pattern of bacterial uropathogens isolated from the patients with CAUTIs in an attempt to help authorities to formulate antibiotic prescription policies.

Materials and Methods: Aseptically collected midstream urine samples from symptomatic UTI patients attending Outpatient Department of this tertiary care hospital were subjected to microbiological analysis. After semi quantitative culture, the responsible bacteria with significant colony count were identified by biochemical tests and Vitek 2 automated system. Antimicrobial susceptibility testing of the isolated uropathogens was performed by modified Kirby Bauer's disc diffusion method in accordance with the recommendations of the Clinical and Laboratory Standards Institute.

Result: Of the 269 isolated uropathogens, *Escherichia coli* was found to be the predominant one comprising 50.93% of the total isolates followed by *Klebsiella pneumoniae* (20.07%) and *Enterococcus faecalis* (14.13%). The isolated *E. coli* were highly sensitive to gentamicin (90.51%), nitrofurantoin (87.59%), imipenem (87.59%), and piperacillin-tazobactum (85.4%). However, only 58.39% and 49.64% of isolated *E. coli* were sensitive to ciprofloxacin and cotrimoxazole, respectively. Regarding Gram-positive cocci, a high potency of nitrofurantoin, vancomycin, and linezolid against them was observed.

Conclusion: The isolated uropathogens exhibited higher resistance to commonly used oral antibiotics such as ciprofloxacin, cotrimoxazole, amoxicillin-clavulanate, and cefazolin. Since they exhibited high-level sensitivity to oral antibiotic nitrofurantoin apart from parenterally used antibiotics, use of nitrofurantoin can be emphasized as a first line treatment option for treating the patients suffering from CAUTI in this region.

Key words: Antimicrobial sensitivity, Community-acquired urinary tract infection, Nitrofurantoin, Uropathogens

INTRODUCTION

Urinary tract infection (UTI) is a very common clinical condition forcing the people in the community to seek medical care and accounts for considerable morbidity and health costs. Worldwide, about 150 million people are diagnosed with UTI each year, costing the global economy in excess of 6 billion US dollars.[1] UTI in adult patients should be considered uncomplicated if the patient is not pregnant or elderly, if there has been no recent instrumentation or antimicrobial treatment, and if there is no known functional or anatomical abnormalities of genitourinary tract.

However, there is a common practice to treat community-acquired uncomplicated UTI empirically by oral antibiotics before the availability of urine culture sensitivity report. Infectious Diseases Society of America guidelines state that uncomplicated UTI in women should be treated empirically

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with cotrimoxazole, unless the community resistance among uropathogens exceeds 10-20%. Alternative therapy for uncomplicated UTI includes a fluoroquinolone, nitrofurantoin, or fosfomycin, wherever cotrimoxazole resistance is >10-20%.[2] However, the etiology of UTI and the antibiotic susceptibility of uropathogenes vary with time and locations challenging the physician to treat such condition. Thus, the diagnosis and empirical treatment of Community-acquired UTI (CAUTI) in an outdoor setting is challenging, and it is wise to select an appropriate antibiotic based on the knowledge of the prevalent uropathogens and their resistance pattern in the community.

This study has been performed to find out the present uropathogen profile responsible for CAUTI among the people attending Outpatient Departments (OPD) of this institution and their antibiotic susceptibility patterns in an attempt to formulate guidelines to treat CAUTI in this region.

MATERIALS AND METHODS

The present study was performed for a period of 1-year on the patients attending OPD of this tertiary care hospital with signs and symptoms suggestive of UTI.

Aseptically collected freshly voided midstream urine samples were submitted to the microbiology laboratory. The samples were processed immediately, and semi quantitative urine culture was performed on MacConkey's agar and sheep blood agar using calibrated loop and plates were incubated overnight at 37°C. Significant bacteriuria was defined as a culture of bacterial species from the urine sample at a concentration of $\geq 10^5$ cfu/mL as per the recommendation of Kass.[3] The culture report was supported by microscopy of urine showing presence of leucocytes at least 10^4/ml. The isolated organisms were identified by standard biochemical tests and using Vitek 2 automated system.

Antimicrobial susceptibility testing of isolated bacteria was done on Mueller-Hinton agar with commercially available discs by modified Kirby Bauer's disc diffusion method, and the results were interpreted according to Clinical and Laboratory Standards Institute guidelines.[4]

RESULTS

A total of 269 bacteria were isolated from 258 patients attending OPD with signs and symptoms suggestive of UTI.

Out of 269 uropathogens, 226 (84.01%) were Gram-negative bacilli, and the rest were Gram-positive cocci (15.99%). *Enterobacteriaceae* constituted the majority of Gram-negative bacilli isolated, and the remaining were *Pseudomonas aeruginosa* and *Stenotrophomonas maltophilia*. Isolated Gram-positive cocci consisted of *Enterococcus faecalis*, *Staphylococcus aureus,* and *Staphylococcus saprophyticus*. *Escherichia coli* was the predominant bacteria isolated, and the frequency of isolation of other bacteria has been shown in Table 1.

Tables 2 and 3 show the antibiotic susceptibility pattern of isolated *Enterobacteriaceae* and Gram-positive cocci.

Isolated *E. coli* were highly sensitive to nitrofurantoin, gentamicin, piperacillin-tazobactum, and imipenem, whereas they exhibited relatively higher resistance to commonly used oral antibiotics such as cotrimoxazole, ciprofloxacin, cefazolin, and amoxicillin-clavulanate. Isolated *P. aeruginosa* were highly sensitive to piperacillin-tazobactum (80.95%), imipenem (90.48%), and colistin (95.24%). 52.38% and 14.28% of isolated *P. aeruginosa* were sensitive to ciprofloxacin and cotrimoxazole, respectively. Regarding Gram-positive cocci, a high potency of nitrofurantoin, vancomycin, and linezolid against them was observed.

Table 1: Distribution of bacteria isolated from CAUTI (*n*=269)

Bacteria isolated	Number	Percentage
Escherichia coli	137	50.93
Klebsiella pneumoniae	54	20.07
Enterococcus faecalis	38	14.13
Pseudomonas aeruginosa	21	7.81
Enterobacter aerogenes	4	1.49
Citrobacter spp.	4	1.49
Proteus mirabilis	3	1.12
Stenotrophomonas maltophilia	3	1.12
Staphylococcus saprophyticus	3	1.12
Staphylococcus aureus	2	0.74

CAUTI: Community-acquired urinary tract infection

Table 2: Antibiotic susceptibility of isolated *Enterobacteriaceae*

Antibiotics	Percentage of bacteria susceptible			
	Escherichia coli	*Klebsiella pneumoniae*	Others	Total
Nitrofurantoin	87.59	70.37	81.82	82.67
Cotrimoxazole	49.64	50	63.64	50.5
Ciprofloxacin	58.39	42.6	36.36	52.97
Gentamicin	90.51	62.97	72.73	82.18
Amoxicillin-clavulanate	32.12	18.52	18.18	27.72
Cefazolin	39.42	38.89	36.36	39.11
Ceftriaxone	54.74	35.19	72.73	50.5
Piperacillin-tazobactum	85.4	64.81	81.82	79.7
Imipenem	87.59	85.19	100	87.62
Doxycycline	51.82	42.59	27.27	48.02

Table 3: Antibiotic susceptibility of isolated Gram-positive bacteria

Antibiotics	Percentage of bacteria susceptible		
	Enterococcus faecalis	*Staphylococcus saprophyticus*	*Staphylococcus aureus*
Nitrofurantoin	100	100	100
Amoxicillin	28.95	0	0
Amoxicillin-clavulanate	84.21	66.67	100
Ciprofloxacin	55.26	66.67	100
Doxycycline	36.84	66.67	50
Gentamicin	-	100	50
Cotrimoxazole	-	66.67	100
Vancomycin	97.37	100	100
Linezolid	100	100	100

DISCUSSION

This study demonstrated that *E. coli* was the predominant pathogen isolated from patients with CAUTI constituting 50.93% of total isolates. However, the proportion of their isolation was slightly lower than those described in various studies conducted in India,[5,6] as well as worldwide.[7,8] *Klebsiella pneumoniae* was the second most common bacteria isolated constituting 20.07% of total isolates. This finding was almost similar to the various studies from India.[5,6] In this study, Gram-positive cocci were responsible for a considerable number of cases where *E. faecalis* accounted for 14.13% of total isolates. Their proportion was much higher than those observed in various studies.[5]

Our study clearly showed that there was the high resistance of isolated *E. coli* to commonly used oral antibiotics such as cotrimoxazole, fluoroquinolone, cefazolin, and amoxicillin-clavulanate. This finding is similar to previous community-based studies in India.[5,9,10] Scenario from worldwide has demonstrated that resistance rates for cotrimoxazole among *E. coli* with uncomplicated UTI range from 11% in scandinavian countries to 34% in Spain and Portugal.[11] Arslan *et al.* reported 36% resistance to cotrimoxazole and 17% resistance to fluoroquinolones in Turkey.[12] Kashef *et al.* demonstrated that only 38.2% of E. coli isolates were susceptible to Cotrimoxazole.[7] The variability among different centers confirms the need for availability of local resistance prevalence data to select appropriate antibiotic to treat empirically such condition.

The high sensitivity of *E. coli* to antibiotics such as nitrofurantoin, gentamicin, piperacillin-tazobactum, and imipenem was similar to the findings of Kothari and Sagar from India.[4] Despite the fact that nitrofurantoin has poor activity against *Proteus* spp, which constituted very small portion of uropathogen in this study, this drug has exhibited good coverage against both Gram-positive and Gram-negative isolates. Previous Indian studies have also shown lower resistance rates of uropathogens to this drug.[9,10] Hence, this antimicrobial agent can be considered as a first-line treatment option for CAUTI in this geographical area.

Increasing resistance of uropathogens of CAUTI to commonly used oral antibiotics is an alarming scenario. There is a common practice to treat CAUTI empirically without the guidance of urine culture sensitivity report. But, this treatment should follow the prevalent uropathogens in that community and their antibiotic susceptibility pattern. Otherwise injudicious use of antibiotics will help the resistant strains to emerge. In an attempt to prevent the emergence of resistant strains, periodic surveillance is necessary to find out prevalent uropathogens in that geographical area with their antibiogram. This will help authorities to formulate antibiotic prescription policies.

CONCLUSION

This study has clearly demonstrated *E. coli* as predominant uropathogen responsible for CAUTI in this geographical area along with high resistance of isolated uropathogens to antibiotics such as cotrimoxazole, ciprofloxacin, cefazolin, amoxicillin-clavulanate, and good coverage of nitrofurantoin against the majority of uropathogens. Thus oral administration of nitrofurantoin can be considered as a first-line treatment option for CAUTI in this region. Along with this periodic surveillance should be carried out to update the guideline for the treatment of CAUTI.

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Original Article

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Prevalence of Risk Factors and its Association with Non-Communicable Disease among the Faculty Members of Teaching Institute of Ahmedabad City, Gujarat: A Cross-Sectional Study

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Abstract

Background: Changing life style has been long associated with the development of many chronic diseases. Annual toll of 16 million people is dying prematurely due to non-communicable diseases (NCDs), according to a new WHO report. This study was aimed to know the prevalence of risk factors and its association with NCDs. It was a cross-sectional study among the faculty members (25-64 years of age) of teaching institutes and conducted in colleges and schools of Ahmedabad city of Gujarat.

Materials and Methodology: A semi-structures questionnaires, mercury sphygmomanometer, anthropometric measurements using standard procedure used as a study tool.

Results: The prevalence of risk factors such as smoking, use of smokeless tobacco, and alcohol consumption was as follow: 5.21, 12.15, and 5.90, respectively. The disease-specific prevalence for males' versus females' were: 23.40 versus 26.38, 4.51 versus 3.10, 30.55 versus 22.91, and 10.41 versus 7.29 for hypertension, diabetes, overweight, and obesity, respectively. Risk factors with the increase odds ratio for NCDs were: Tobacco consumption, job stress, physical inactivity, overweight, and obesity.

Conclusion: The higher prevalence of risk factors for NCDs even a high sophisticated background needs intervention programs and public health education approach.

Key words: Association, Non-communicable disease, Prevalence, Risk factors

INTRODUCTION

Non-communicable diseases (NCDs), such as heart and lung disease, stroke, cancer, and diabetes, have been leading cause of morbidity and mortality in almost all of countries. According to WHO, near about 16 million people dying prematurely due to NCDs.[1] Having of risk factors such as tobacco use, physical inactivity, unhealthy diet, and the harmful use of alcohol and some medical conditions such as hypertension and diabetes increases the risk of development of NCDs. Tobacco use and being overweight are responsible for the death of at least 5 million and 2.8 million people, respectively, every year and, almost 7.5 million die because of having high blood pressure.[2] In the country like India, NCDs are not affordable in terms of human suffering, as well as the cost of treatment. Early detection can save the high cost of treating such NCDs when it is still relatively cheap to manage.[3]

Usually, teacher's habit and lifestyle behavior at school or college are well-observed by students. If the teachers are free from risk factors, only then positive role modeling may transmit to their students. This study aims to determine the prevalence of risk factors and its association with NCDs among the faculty members of teaching institute of the Ahmedabad city.

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MATERIALS AND METHODOLOGY

Sample Size

The sample size of 576 faculty members was calculated with allowable error 10% using the prevalence rate (41%) of any risk factors for NCDs found out during the pilot study.

Study Period

From July 2012 to August 2013.

Study Design

It was a cross-sectional study.

Study Area

The study was done in schools/colleges of Ahmadabad city.

Study Population

Total 288 male and 288 female faculty members from schools/colleges of Ahmedabad were included in the study.

Data Collection

List of schools and colleges of Ahmadabad received from District Office and the use of the internet. Cluster random sampling was used to collect sample data from six zones of Ahmadabad Municipal Corporation. Each zone of Ahmedabad was considered as a cluster and 96 faculty members, 48 males, and 48 females were taken as a study population from each zone and thus data from 576 faculty members collected. Schools/colleges from each zone selected randomly using the random number table. All the available teaching staff from randomly selected school/college interviewed with the permission of the principal or in charge head of the institute. Before collecting the data, informed consent was taken from study participants. The study population assured that information given by them would be kept confidential.

Study Tool

Data collected through interview with the help of structured questionnaire among the person age between 25 and 64 years age. Fruit and vegetable intake were measured using standard serving size. Physical measurement of the respondents was done using scientific instruments. Data entered in excel sheet and analyzed with the help of Microsoft Excel and Epi info7.1.2 software.

RESULT

Baseline Information of Study Participants

42.54% of study participants belonged to 45-54 years of age group. The mean age of male and female was 45.47 years and 42.76 years, respectively.

Distribution of Risk Factors of NCDs

Out of 288 male faculty members, prevalence of smoking, smokeless tobacco, and alcohol consumption were 15 (5.21%), 35 (12.15%), and 17 (5.90%), respectively. The prevalence of smoking and smokeless tobacco was higher in the age group of 45-54 years than another age group. Consumption of alcohol was higher in the age group of 35-44 years (10.00%). All the 288 female faculty members were lifetime abstainer for tobacco and alcohol consumption (Table 1).

The mean number of servings of fruit was 1.95 for male faculty members and 2.47 for female faculty members and of vegetable it was 2.80 for male faculty members and 2.63 for female faculty members. 229 (79.51%) males and 218 (75.60%) females involved themselves in various types of physical activity including jogging, cycling, running, swimming, meditation or pranayama, etc., for 150 min/week. Male faculty members were more overweight and obese (30.55% and 10.41%, respectively) as compared to female (22.91% and 7.29%, respectively). The prevalence of job stress was higher in female faculty members (16.66%) as compared to male faculty members (8.34%), and the difference was statistically significant ($\chi^2 = 9.14$, $P < 0.05$). The result also revealed that total prevalence of hypertension was found to be 23.26% among male faculty members and 26.38% in female faculty members. Among hypertensive, 34 (11.79%) males and 45 (15.62%) females had self-reported hypertension and rest of them 33 (11.45%) males and 31 (10.76%) females detected with high blood pressure during the study. 75 (26.04%) females versus 127 (44.09%) males tested for diabetes in last 1 year. 13 (4.51%) males and 9 (3.10%) females had self-reported diabetes and the majority of them belonged to the age group of 45-54 years (Table 2).

81 out of 288 (28.12%) males and 87 out of 288 (30.20%) females were suffering from different kind of NCDs and majority of them having hypertension (Table 3).

Among males, positive family history was about six times likely to have diabetes as compared to negative family history ($P = 0.001$, odd ratio (OR) = 6.65, and 95%

Table 1: Age distribution of tobacco and alcohol consumer - (male)

Age-groups (in years)	*n* (%)			
	Current smoking	Current users of smokeless tobacco	Alcohol consumption	Total
25-34	2 (5.89)	4 (11.77)	3 (8.82)	34 (100)
35-44	2 (2.22)	10 (11.11)	9 (10.00)	90 (100)
45-54	11 (8.67)	21 (16.53)	3 (2.36)	127 (100)
55-64	0	0	2 (5.40)	37 (100)
Total	15 (5.21)	35 (12.15)	17 (5.90)	288 (100)

confidence interval (CI) 2.12-20.81) while among females, positive family history was about eleven times likely to have diabetes as compared to negative family history ($P = 0.001$, OR = 11.28, and 95% CI 2.71-46.88) (Table 4).

Table 2: Gender wise distribution of risk factors of NCDs

Characteristic	Male (*n*=288)	Female (*n*=288)
Fruits and vegetable consumption		
Mean number of serving of fruits consumed	1.95	2.47
Mean number of serving of vegetables consumed	2.80	2.63
Details of exercise		
Percentage of study population involved in 150 min/week moderate to severe activity (walking, cycling, yoga, pranayam)	77.08	61.54
Physical measurement		
Percentage who are overweight (BMI≥25 kg/m^2)	30.55	22.91
Percentage who are obese (BMI≥30 kg/m^2)	10.41	7.29
Job stress		
Percentage of study population having job stress	8.34	16.66
Details of hypertension		
Percentage of self-reported cases of hypertension (SBP≥140 and/or DBP≥90)	11.79	15.62
Percentage of new cases detected during survey (hidden cases)	11.45	10.76
Details of diabetes		
Percentage of self-reported cases of diabetes	4.51	3.10

NCDs: Non-communicable diseases, BMI: Body mass index, SBP: Systolic blood pressure, DBP: Diastolic blood pressure

Table 3: Prevalence of non-communicable disease among study participants

Medical condition	Male (*n*=288) (%)	Female (*n*=288) (%)	Total (%)
Hypertension	67 (82.81)	76 (87.35)	143 (85.11)
Self-reported cases of diabetes	9 (11.11)	0	9 (5.35)
Hypertension+diabetes	4 (4.93)	9 (10.34)	13 (7.73)
Self-reported cases of cancer	1 (1.23)	2 (2.46)	3 (1.78)
Total cases of NCDs	81 (100)	87 (100)	168 (100)

NCDs: Non-communicable diseases

Table 4: Association between family history, hypertension, and diabetes

Medical condition	Family history positive (*n*)	Odds ratio	95% CI
For male faculty members			
Hypertension	16	1.85	0.94-3.63
Diabetes	7	6.65	2.12-20.81
For female faculty members			
Hypertension	20	1.53	0.82-2.84
Diabetes	6	11.28	2.71-46.88

CI: Confidence interval

The odds ratio of developing NCDs among male faculty members who consumed tobacco was 2.96 times more ($P = 0.006$, OR = 2.96, and 95% CI 1.49-5.14). The similar significant association found between job stress and NCDs development ($P = 0.002$, OR = 3.69, and 95% CI 1.57-8.64). The odds ratio of developing NCDs were 2.49 and 2.28 times higher in female faculty members significantly who had job stress ($P = 0.005$, OR = 2.49, and 95% CI 1.31-4.75) and were overweight and obese ($P = 0.002$, OR = 2.28, and 95% CI 1.37-3.94), respectively (Table 5).

DISCUSSION

576 faculty members (50% males vs. 50% females) from different schools/colleges included as study participants. 280 (97.23%) males and 270 (93.75%) females were married, and rests of them were unmarried. Teacher's ages ranged from 25 to 64 years with mean age of female were 42.76 years, and that of a male was 45.47 years. Ibrahim *et al.*, also observed compatible demographic profile in which males were 52.8% and females were 47.2% of total study population and teacher's age ranged from 22 to 60 years with a mean of 36.52 ± 7.62 and among them majority were married (83.7%).[4]

The prevalence of smoking, use of smokeless tobacco, and alcohol consumption found 5.21%, 12.15%, and 5.90%, respectively, in our study which is quite lower than the same found in Kerala (smoking 42% and alcohol consumption 26%) and Gandhinagar (smokeless tobacco consumption 23.1%).[5,6] Increased awareness regarding harmful effect of tobacco use was responsible for the lower prevalence of habit related behavior. We cannot rule out less reporting of alcohol consumption as Gujarat is a dry state (Table 1).

WHO/FAO recommends intake of a five servings or 400 g of green leafy vegetables and fruits consumption daily for the prevention of NCDs.[7] Our study revealed that men and women were consuming fewer amounts of fruit and vegetables than the recommended (average consumption, for male; 2.80 servings of vegetables and 1.95 servings of fruits in a day and for female; 2.63 servings of vegetables, and 2.47 servings of fruits in a day) (Table 1).

Females (38.46%) were more physically inactive as compared with males (22.92%), and the result was comparable with the findings given by Basu and Biswas (physical inactivity found 38.6% in females and 38.4% in males).[8] The double responsibility of the job and also domestic housework may be responsible for higher physical inactivity among female participants. 30.55% males versus 22.91% females and 10.41% males versus 7.29% females found overweight and obese, respectively, in our study which was fewer when

Table 5: Association of various risk factors with development of non-communicable disease (total NCDs cases among male=81 and among female *n*=87)

Variables	Male			Female		
	Odds of NCDs+ nt/-nt	*P* value	95% CI	Odds of NCDs+ nt/−nt	*P* value	95% CI
Tobacco consumption yes/no	2.96	0.006	1.49-5.14	-	-	-
Vegetable and fruits serving (<5 servings/≥ 5 servings)	-	-	-	-	-	-
Physical activity - min/week (<150 min/week/≥150 min/week)	0.24	0.001	0.13-0.43	0.51	0.012	0.30-0.86
Job stress yes/no	3.69	0.002	1.57-8.64	2.49	0.005	1.31-4.75
Overweight and obese yes/no	-	-	-	2.28	0.002	1.37-3.94

NCDs: Non-communicable diseases, CI: Confidence interval

compared with teachers of Western Saudi Arabia.[9] Serious concern should be taken as overweight and obese is a sign of physical inactive.

According to our survey, females were at more risk of getting hypertension (26.38) as compared to males (23.24%) but contradictory findings shown in the study done in Nepal in which male were prone to get hypertension (Table 3).[10] The prevalence of diabetes found almost equal among both the study group. The findings Alabdouli *et al*., also supported by our findings that family history associated with the occurrence of diabetes (Table 4).[11]

Smoking, smokeless tobacco chewing, overdose of alcohol, unhealthy diet, physical inactivity, and overweight/obesity are modifiable risk factors for the development of NCDs, according to WHO.[12] The same finding observed in our study that use of tobacco, job stress, and overweight and obesity attributed for the development of NCDs.

CONCLUSION

The high prevalence of modifiable risk factors of NCDs was present even in the high socio-economical background. Hidden cases of hypertension revealed that lack of health seeking behavior among faculty members. The risk factors such as physical inactivity, tobacco use, overweight, obesity, and job stress needs sound public health education.

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Original Article

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Assessment of Focal Parenchymal Abnormalities in Cerebral Venous Thrombosis with Diffusion Weighted Imaging

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Abstract

Introduction: Parenchymal swelling without abnormalities in attenuation or signal intensity on images may occur in as many as 42% of patients with cerebral venous thrombosis (CVT). Sulcal effacement, diminished cistern visibility, and a reduction in ventricular size may occur. Focal brain abnormalities have been identified in as many as 57% of patients with CVT.

Materials and Methods: A 30 patients who were found to have CVT on magnetic resonance imaging (MRI) and magnetic resonance venography during the period from August 2013 to November 2014 were included in this study. All patients were evaluated with a 1.5T MRI 8 channel GE BRIVO MRI Machine. Sequences used were axial and sagittal T1, axial and coronal T2, axial fluid-attenuated inversion recovery (FLAIR), axial T2*, two-dimensional time-of-flight, and axial diffusion weighted imaging (DWI). DW images and apparent diffusion coefficient (ADC) maps were evaluated for increased, decreased, or unchanged signal intensity.

Results: 22 (73.3%), out of 30 patients, were found to have focal parenchymal changes in the form of T2 and FLAIR hyperintensity and T1 hypointensity affecting gray matter/white matter/or both. They were characterized conventionally as hemorrhagic venous infarcts in 16 (53.3%) patients and as non-hemorrhagic venous infarcts in 6 (20%) patients with above-mentioned sequences and also T2* weighted images based on presence or absence of hemorrhage. Using DWI and ADC maps, these focal parenchymal abnormalities were characterized as either cytotoxic or vasogenic edema. 12 (40%) patients were found to have both cytotoxic and vasogenic edema, 9 (30%) patients purely vasogenic edema, and 1 (3.3%) patient purely cytotoxic edema. Hemorrhage was associated with both cytotoxic and vasogenic edema.

Conclusion: Focal parenchymal changes in CVT may be secondary to cytotoxic edema, vasogenic edema, or intracranial hemorrhage. Vasogenic and cytotoxic edema patterns may coexist. Hemorrhage may occur with both types of edema, and various patterns may coexist in the same region.

Key words: Cytotoxic edema, Magnetic resonance imaging, Vasogenic cerebral edema, Venous thrombosis

INTRODUCTION

Parenchymal changes in cerebral venous thrombosis (CVT) could be either diffuse cerebral edema cases or focal parenchymal changes. The focal parenchymal changes have conventionally been labeled as venous infarcts and further classified as hemorrhagic or non-hemorrhagic based on the presence of hemorrhage. The predominant conventional magnetic resonance imaging (MRI) findings of CVT are hyperintense parenchymal abnormalities on a T2-weighted image that involve gray matter, white matter, or both in approximately 50-60% of patients and intraparenchymal hematoma in approximately 35-40%. The pathophysiology of CVT remains unclear. Both vasogenic and cytotoxic edema are thought to occur in the setting of CVT. Increased venous pressure may cause breakdown of the blood-brain barrier and vasogenic edema or may cause reduced cerebral blood flow and cytotoxic edema.

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Unlike conventional MR images, diffusion weighted (DW) MR imagescan differentiate between vasogenic and cytotoxic edema. DW images are sensitive chiefly to the molecular diffusion of water molecules. Cytotoxic edema is characterized by markedly decreased diffusion. Vasogenic edema, with increased interstitial water, demonstrates increased diffusion. We sought to characterize focal parenchymal changes associated with CVT with DW imaging (DWI) and to determine whether this technique could differentiate lesions that would resolve from those that would lead to permanent injury.

MATERIALS AND METHODS

The study was performed in the Department of Radiodiagnosis, Mysore Medical College and Research Institute, Mysore on patients who were found to have CVT on MRI and magnetic resonance venography (MRV).

Sample size: 30 cases

Type of study: Explorative study.

Study period: 15 months from August 2013 to November 2014.

Imaging

All patients were evaluated with a 1.5T MRI 8 channel GE BRIVO MRI Machine. Sequences used were axial and sagittal T1, axial and coronal T2, axial fluid-attenuated inversion recovery (FLAIR), axial T2*, two-dimensional time-of-flight (2D-TOF), and axial DWI. DW images were obtained by using single-shot, spin-echo echo-planar imaging with a sampling of the entire diffusion tensor with six non-linear directions. Six high-b-value images corresponding to the six non-linear directions were acquired followed by a single low-b-value image. Imaging parameters included 6000/92 (TR/TE), a field of view (FOV) of 22 cm × 22 cm, image matrix of 128 × 128 pixels, section thickness of 5 mm and 2 signal averages. Apparent diffusion coefficient (ADC) maps were also generated. T1-weighted sagittal images were acquired with 340/10, 20 cm × 20 cm FOV, an acquisition matrix of 256 × 192 pixels, section thickness of 5 mm, and 2 signal averages. FLAIR axial MR images were obtained with 8013 × 80.5 (TR/TE), 22 × 25 cm FOV, acquisition matrix of 288 × 224 pixels, section thickness of 5 mm, and 2 signal averages. Fast spin-echo T2-weighted MR axial images were obtained with 3732/90, 22 × 22 cm FOV, acquisition matrix of 256 × 256 pixels, section thickness of 5 mm, and 2 signal averages. T2* axial images were obtained with 680 × 26 (TR/TE), 22 cm × 16.5 cm FOV, section thickness of 5 mm, and acquisition matrix of 256 × 192 pixels. The 2D TOF sequence was done in the sagittal plane, and then the source images were reconstructed into three-dimensional maximum intensity projection images.

Image Analysis

The presence of CVT in the cases was confirmed by loss of flow void in the sinuses on conventional sequences and absence of flow on MRV. Focal parenchymal abnormalities were detected on the basis of increased signal on T2 weighted and FLAIR images. The presence of hemorrhage was assessed using both conventional and T2* images. DW images and ADC maps were inspected visually, and signal intensity of focal parenchymal changes was assessed as increased, decreased, or unchanged in comparison to that of the contralateral, normal appearing brain.

RESULTS

In the present study, there was found to be a slight female preponderance with 53.3% of the patients being females (Chart 1). The mean age of the patients was found to be 35.3 years, with the mean age of the female patients being 29 years, whereas the mean age of the male patients was 42.5 years. 22 (73.3%), out of 30 patients, were found to have focal parenchymal changes in the form of T2 and FLAIR hyperintensity and T1 hypointensity affecting gray matter/white matter/or both. They were characterized conventionally as hemorrhagic venous infarcts in 16 (53.3%) patients and as non-hemorrhagic venous infarcts in 6 (20%) patients (Table 1) with above-mentioned sequences and also T2* weighted images based on presence or absence of hemorrhage. Using DWI and ADC maps these focal parenchymal abnormalities were characterized as either cytotoxic or vasogenic edema (Table 2). 12 (40%) patients were found to have both cytotoxic and vasogenic edema (Figure 1), 1 (3.3%) patient had purely cytotoxic edema (Figure 2), and 9 (30%) patients purely vasogenic

Table 1: Distribution of patients with CVT depending on parenchymal changes

Focal parenchymal changes	Number of cases	Percentage
Absent	8	26.6
Hemorrhagic infarct	16	53.3
Non-hemorrhagic infarct	6	20
Total	30	100

CVT: Cerebral venous thrombosis

Table 2: Distribution of patients with CVT depending on DWI

Type of Edema	Number of cases	Percentage
Pure vasogenic	9	30
Co-existent	12	40
Pure cytotoxic	1	3.3

CVT: Cerebral venous thrombosis, DWI: Diffusion weighted imaging

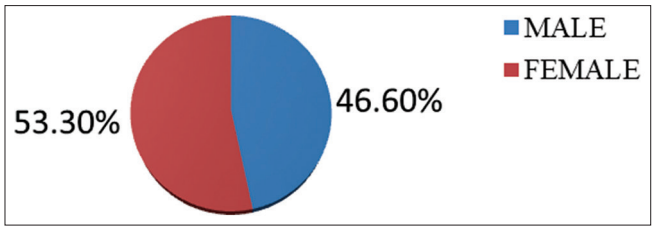

Chart 1: Sex distribution

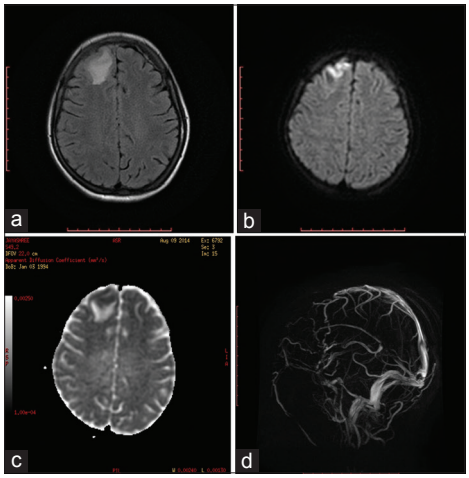

Figure 1: (a-d) Axial fluid-attenuated inversion recovery image showing hyperintense signal involving both gray and white matter in right frontal lobe. Diffusion weighted images show hyperintense signal involving only the gray matter. The white matter appears isointense to a corresponding white matter of left hemisphere. Apparent diffusion coefficient map shows hypointense signal involving gray matter implying cytotoxic edema, whereas hyperintense signal is seen to involve the white matter suggestive of vasogenic edema. Magnetic resonance venography maximum intensity projection image showing thrombosis of anterior part of superior sagittal sinus

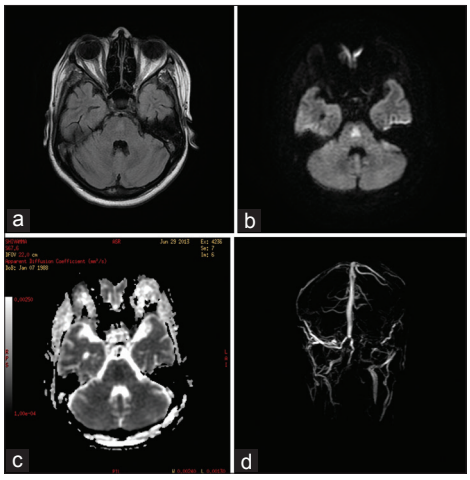

Figure 2: (a-d) Axial T2-fluid-attenuated inversion recovery image showing hyperintense signal in pons. Diffusion weighted images show hyperintense signal in corresponding region with apparent diffusion coefficient map shows hypointense signal in corresponding region suggestive of pure cytotoxic edema. Magnetic resonance venography maximum intensity projection image shows thrombosis of left transverse sinus

edema (Figures 3 and 4). Hemorrhage was associated with both cytotoxic and vasogenic edema.

DISCUSSION

The conventional MRI findings of CVT hyperintense parenchymal abnormalities on a T2-weighted image that involve gray matter, white matter, or both in approximately 50-60% of patients and intraparenchymal hematoma in

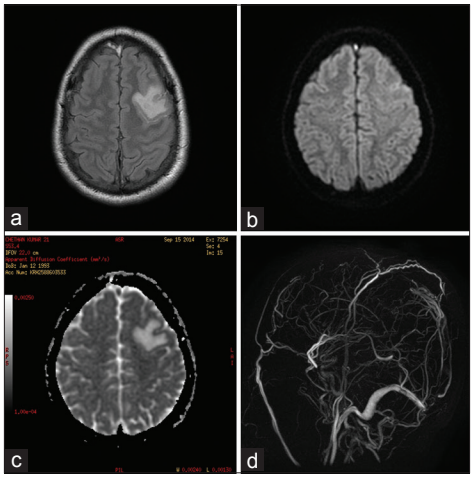

Figure 3 (a-d): Axial T2-fluid-attenuated inversion recovery image showing hyperintensity involving white matter in left frontal lobe region. Diffusion weighted images show no altered signal intensity in corresponding region. Hyperintensity noted in corresponding region in apparent diffusion coefficient map suggestive of pure vasogenic edema. Magnetic resonance venography maximum intensity projection showing absence of flow in superior sagittal sinus

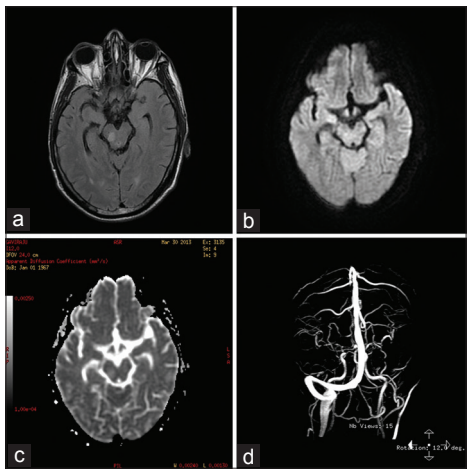

Figure 4: (a-d) Axial T2-fluid-attenuated inversion recovery image shows focal hyperintense signal in midbrain on right side. Diffusion weighted images show no alteration of signal in corresponding region with apparent diffusion coefficient map showing hyperintense signal in corresponding region suggestive of pure vasogenic edema. Magnetic resonance venography maximum intensity projection image shows thrombosis of right transverse sinus

approximately 35-40%.[1] Simonds and Truwit[2] observed non-hemorrhagic infarction in 40% and hemorrhagic infarction found in 26.7%. In a study conducted by Khandelwal *et al*.,[3] hemorrhagic infarcts were the most frequent parenchymal lesions, seen in 60% of cases; non-hemorrhagic infarcts were seen in 13.3% of cases.

In the present study, the most common focal brain abnormality was a hemorrhagic infarction found in 53.3% cases followed by non-hemorrhagic infarction in 20% of cases.

In contrast with arterial ischemic states, many parenchymal abnormalities secondary to venous occlusion are reversible.

Although some T2 hyperintense parenchymal abnormalities resolve, others persist and indicate permanent tissue injury. Lesion distribution does not differentiate between these two lesion types. T2 hyperintensities maybe secondary to cytotoxic edema or vasogenic edema. Vasogenic and cytotoxic edema patterns may coexist.[4]

Hemorrhage may occur with both types of edema, and various patterns may coexist in the same region. In view of the variable nature of the parenchymal abnormalities that may occur in CVT, the use of the term venous infarct in reference to these lesions should be discouraged because that term implies irreversibility.[5]

Unlike conventional MR images, DW MR images can differentiate between vasogenic and cytotoxic edema. As cytotoxic edema due to acute stroke develops, ADC values decrease. The current predominant theory to describe this phenomenon involves loss of ionic gradients with net translocation of water from the extracellular to the intracellular space where water movement is more restricted. Cytotoxic edema produces hyperintensity on DW images and hypointensity on ADC images. In contrast, vasogenic edema leads to increased water in the extracellular space where water is less restricted and is characterized by ADC values that are increased compared with those of normal brain tissue. Because DW imageshave both T2 and diffusion components, vasogenic edema may appear hypointense, isointense, or slightly hyperintense on DW images, but it always produces hyperintensity on ADC images.[6]

In a study by Mullins *et al*., they found that found that DWI, in combination with the clinical history (i.e. seizure), may be useful in differentiating parenchymal lesions that resolve from those that progress to permanent injury in the setting of acute CVT. In their retrospective cohort, lesions with elevated diffusion resolved, lesions with decreased diffusion resolved when the patient had seizures, and lesions with decreased diffusion in the absence of clinical seizure demonstrated abnormality on follow-up images. The ADC values were similar between the lesions with low ADC values that resolved and the lesions with low ADC values that persisted. Lesions characterized by elevated diffusion that showed essentially no abnormality on follow-up images were likely to represent vasogenic edema that is produced in CVT owing to increased pressure in the post-capillary venules and the opening of tight junctions. Lesions characterized by decreased diffusion that showed no abnormality on follow-up images in patients with seizure activity was possibly due to cytotoxic edema. The decreased ADC values in these patients may have resulted from the seizure activity. Animal and human studies have demonstrated decreased ADC values in cortical and white matter lesions in subjects with status epilepticus. The pathophysiology for decreased ADCs in epilepsy is not completely clear. Wang *et al*.[7] reported an increase in sodium concentration in rat pyriform cortex during status epilepticus. They suggested that this might result from energy failure of the Na^-/K^- - ATPase pump, and consequent Na^- and water influx.

Alternatively, reversibility of ADC values in these patients could have been unrelated to the seizures. Based on an animal model of CVT in rats, Röther *et al*.[8] noted that an initially decreased ADC was followed by an increased ADC in some parenchymal lesions.

They hypothesize that the major pathophysiologic event in the first 1-2 h is cytotoxic edema. Cytotoxic edema is produced in CVT when increased venous pressure leads to increased intracranial pressure, decreased capillary perfusion pressure, and severely decreased cerebral blood flow. The resultant blood-brain barrier disruption leads to increased extracellular water, rising ADC values, and increasing lesion volumes. Subsequently, recanalization of thrombosed veins or improvement of collateral drainage and recovering metabolism lead to a decrease in lesion volume. Thus, while cytotoxic edema associated with acute arterial stroke is usually irreversible, cytotoxic edema associated with CVT may be reversible if the blood drains through collateral pathways.[9] Lesions characterized by decreased diffusion that showed an abnormality on follow-up images were likely to represent persistent cytotoxic edema followed by tissue infarction. In these cases, there was likely severely decreased blood flow without enough collateral blood drainage to maintain adequate perfusion.

We found that DWI may be useful in differentiating parenchymal lesions that resolve from those that progress to permanent injury in the setting of acute CVT. Of the 22 (73.3%), out of 30 patients, were found to have focal parenchymal changes in the form of T2 and FLAIR

hyperintensity and T1 hypointensity affecting gray matter/white matter/or both. Using DWI and ADC maps these focal parenchymal abnormalities were characterized as either cytotoxic edema, i.e. increased signal on DWI and decreased signal on ADC maps or vasogenic edema, i.e. increased signal on ADC maps. 12 (40%) patients were found to have both cytotoxic and vasogenic edema, 9 (30%) patients purely vasogenic edema, and 1 (3.3%) patient purely cytotoxic edema. Hemorrhage was associated with both cytotoxic and vasogenic edema. This helped in the prognosis and management of the patients.

However, they were a few limitations to our study. Follow-up imaging in the patients was not done, and hence persistence of abnormality in cases with cytotoxic edema was not assessed. Also, areas of hemorrhage may have interfered with an assessment of ADC values. However, areas of hemorrhage based on T2* images were excluded as much as possible to keep this interference to the least.

CONCLUSION

Focal parenchymal changes in CVT may be secondary to cytotoxic edema, vasogenic edema, or intracranial hemorrhage. Vasogenic and cytotoxic edema patterns may coexist. Hemorrhage may occur with both types of edema, and various patterns may coexist in the same region. In view of the variable nature of the parenchymal abnormalities that may occur in CVT, the use of the term venous infarct in reference to these lesions should be discouraged because that term implies irreversibility. Unlike conventional MR images, DW MRimages can differentiate between vasogenic and cytotoxic edema. This information may be important in prospectively determining the severity of the injury, in the determination of prognosis, and in patient management.

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Original Article

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Severe Metabolic Acidosis in Critically Ill Patients and Its Impact on the Outcome; A Prospective Observational Study

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Abstract

Background: Though acid-base abnormalities are common in critically ill patients, the association of metabolic acidosis with their outcome remains uncertain. Though there are many studies on acid-base abnormalities in critically ill patients, the data focusing specifically on severe metabolic acidosis (pH < 7.20) is scanty. This study was carried out in critically ill patients with single severe metabolic acidosis (pH < 7.20) admitted under the Department of General Internal Medicine to JSS Hospital, Mysore, a major tertiary care center.

Materials and Methods: It was a prospective observational study. A total of 100 consecutive critically ill patients (APACHE II score of 18 or more) with single severe metabolic acidosis (pH < 7.20) admitted to the intensive care units (ICUs) of JSS Hospital, Mysore under the Department of General Internal Medicine fulfilling inclusion and exclusion criteria were studied. Arterial blood gas analysis along with other relevant investigations was done within first 24 h of ICU admission. The hospitalization details and progress of the patients were collected from the in-hospital records. Patients were followed-up until the end points, i.e. discharge by the treating physician, discharge against medical advice or in-hospital death and discharge for a referral.

Results: Out of 100 critically ill patients with single severe metabolic acidosis (pH < 7.20), 70 patients expired compared to 30 patients who were discharged from hospital in stable condition. Out of 86 patients, who had lactic acidosis, 69 (80.2%) patients expired compared to 17 (19.8%) patients who were discharged in stable condition. A high anion gap acidosis was found in 69 patients out of which 47 (68.1%) patients had an adverse outcome. A higher base deficit is associated with high mortality (79.4% compared to 20.6%). Out of 55 patients who were put on mechanical ventilator on the first day, 45 (81.8%) patients expired. 37 patients required vasopressor support on admission out of which 34 (91.8%) patients had lactic acidosis.

Conclusions: This study shows a higher mortality in critically ill patients with severe metabolic acidosis. Lactic acidosis and higher base deficit are associated with higher mortality. Patients with lactic acidosis presented with hypotension and required vasopressor support on admission. Monitoring of serum pH, HCO_3^-, lactate, base excess levels may have prognostic and therapeutic implications.

Key words: Acid-base disorders, Critical illness, Metabolic acidosis

INTRODUCTION

Acid-base abnormalities are common in critically ill patients. Acidosis in critically ill patients may occur due to a rise in arterial partial carbon dioxide tension ($PaCO_2$), i.e. respiratory acidosis or due to fixed acids, i.e. metabolic acidosis.[1] There is a difference between patients with respiratory acidosis and those with metabolic acidosis *vis-a-vis* physiological variables and clinical outcomes prompting some researchers to conclude that it is the cause of acidosis rather than the acidosis per se that determines the clinical outcomes.[2,3] Metabolic acidosis may be due to an increase in endogenous acid production (such as lactate and ketoacids), loss of bicarbonate (as in diarrhea), or accumulation of endogenous acids (as in renal failure). Common causes of metabolic acidosis

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include lactic acidosis, hyperchloremic acidosis, renal failure, and ketoacidosis. Metabolic acidosis can be broadly classified based on Anion Gap as normal anion gap metabolic acidosis and high anion gap metabolic acidosis. This classification has therapeutic implications also. Metabolic acidosis is called "severe" when pH < 7.20 (metabolic acidosis with pH < 7.20 is severe metabolic acidosis).[4] Even though metabolic acidosis is common in the intensive care units (ICUs), data on severe metabolic acidosis are scanty.

MATERIALS AND METHODS

It was a prospective observational study (descriptive non-interventional study). Institutional ethics committee approval was obtained. This study was undertaken at JSS Hospital, a tertiary care referral teaching hospital attached to JSS Medical College, a constituent college of JSS University, Mysore, Karnataka State, South India. Written informed consent was obtained in all cases. APACHE score was calculated for each patient on the day of admission to ICU using APACHE II scoring system. Critically ill adult patients above the age of 18 years admitted in ICUs with APACHE II score of 18 or more were considered. Critically ill adult patients above the age of 18 years admitted in ICUs with APACHE II score of 18 or more and who were found to have single severe metabolic acidosis with pH < 7.20 on first 24 h of admission were included for the study. Critically ill patients with single respiratory acidosis and mixed acidosis were excluded. Arterial blood gas (ABG) analysis done within first 24 h of admission into the ICU were taken and patients in critical care areas with single severe metabolic acidosis with pH < 7.20 on first 24 h of admission were enrolled and the following data were noted: Age, gender, presenting symptoms and signs, diagnosis, relevant investigation reports, treatment and intravenous fluids used, duration of stay in ICU and any complications thereof, any new developments in ICU, use of mechanical ventilation and its duration and mortality in the ICU, initial pH levels, initial HCO_3^- levels, serum lactate levels, anion gap, APACHE II score and mortality, etc. This study included 100 such patients during a period of 2 years. Inclusion in the study would not affect the routine patient care in the ICU. Patients were followed up until discharge (from ICU) or death. Quantitative data are represented as mean ± standard deviation. To assess the association among qualitative variables the Chi-square test, *t*-test, and ANOVA were used. Differences were considered statistically significant if $P < 0.05$. Statistical analysis was performed using SPSS version 16.0 for Microsoft windows.

RESULTS

Out of the total 100 patients, a total of 66 patients were males and 34 were females. Mean age of presentation was 59.39 ± 17.05 years for males and 56.41 ± 17.81 years for females. Out of 100 critically ill patients with single severe metabolic acidosis (pH < 7.20), the average pH value was 7.08 with lowest being 6.62 and highest being 7.19. Mean duration of ICU stay was 3 ± 1 day.

Out of total 100 cases who had single severe metabolic acidosis (pH < 7.2) on admission, 70 cases expired, and 30 cases were discharged in stable condition (Figure 1). Severe metabolic acidosis on admission is associated with significant mortality in critically ill patients ($P = 0.001$).

Out of 100 patients, 88 patients had APACHE II score of >20 and 12 patients had APACHE II score between 18 and 20. Of the 88 patients who had APACHE II score more than 20, 64 patients expired (72.7%) compared to 20 patients (27.8%) who were discharged with stable condition (Figure 2) which is statistically significant ($P = 0.001$).

Out of 86 patients who had high lactate levels, 69 (80.2%) patients expired compared to 1 patient out of 13 with

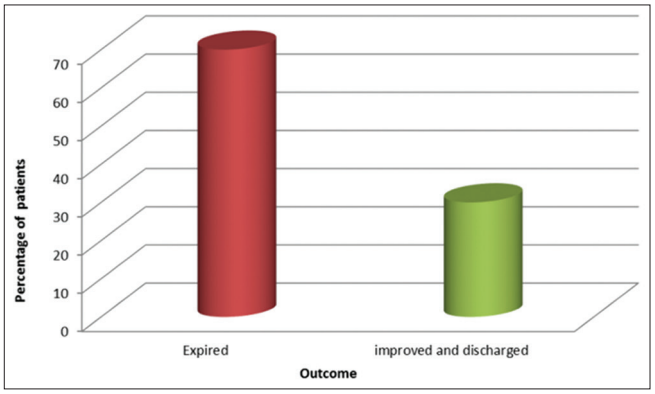

Figure 1: Outcome in severe metabolic acidosis

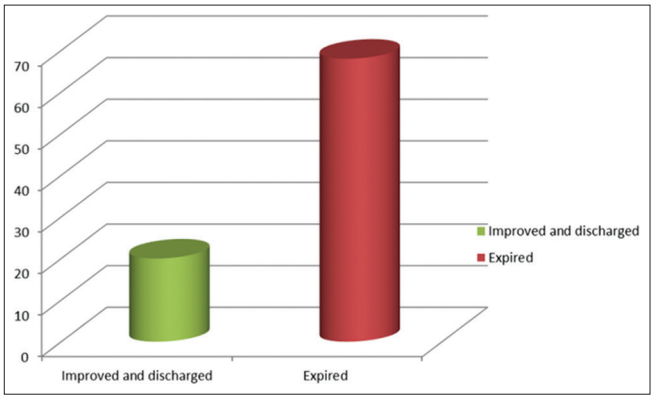

Figure 2: APACHE II score > 20 and outcome

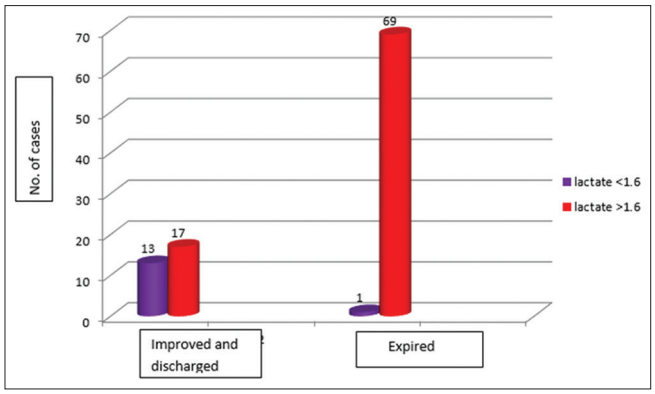

Figure 3: Lactate levels and mortality

normal lactate levels which are statistically significant ($P = 0.04$). Out of 86 patients, who had lactic acidosis, 69 (80.2%) patients expired compared to 17 (19.8%) patients who were discharged in stable condition (Figure 3).

31 patients had normal anion gap severe metabolic acidosis while 69 patients had high anion gap severe metabolic acidosis; There was no statistically significant difference in the outcome of two groups ($P = 0.540$). Out of 100 patients, 68 patients had base excess value <−2. Out of these 68 patients, 54 (79.4%) patients expired compared to 14 (20.6%) patients with normal base excess. The higher mortality was seen in base excess group <−2 compared to normal base excess group, and this was statistically significant ($P = 0.003$). Out of 55 patients who were put on mechanical ventilator on the first day, 45 (81.8%) patients expired compared to 10 (18.2%) patients who did not need mechanical ventilation. Patients who needed mechanical ventilation on admission had significantly higher mortality compared to patients who did not need mechanical ventilator support ($P = 0.04$). Out of 37 patients who required vasopressor support, 34 (91.8%) cases had lactic acidosis and 3 (8.2%) cases were non-lactic acidosis cases. Most common diagnosis in patients with severe metabolic acidosis in the present study was lactic acidosis. Most common diagnosis in patients with lactic acidosis in the present study was sepsis with septic shock. Most common diagnosis in patients with high anion gap non-lactic acidosis was diabetic ketoacidosis, whereas bicarbonate loss from gastrointestinal (GI) tract (acute gastroenteritis [GE]) was common cause of normal anion gap acidosis

DISCUSSION

The term "severe" metabolic acidosis is used when pH is lower than 7.20.[4] Severe metabolic acidosis is not uncommon in critically ill patients. Jung *et al.*[5] reported higher mortality in critically ill patients with severe metabolic acidosis. In the present study, severe metabolic acidosis in critically ill patients was associated with statistically significant mortality, i.e. 70% patients expired compared to 30% patients who were discharged in stable condition ($P = 0.001$) which is consistent with the study by Jung *et al.*[5] Serum lactate levels is an important prognostic marker in metabolic acidosis and when elevated is associated with higher mortality levels as reported by Jung *et al.*[5] Gunnerson[1] compared outcomes in patients with high lactate levels and normal lactate levels and demonstrated significant mortality in patients with high lactate level. Smith *et al.*[6] reported similar findings. In the present study, lactic acidosis is associated with higher mortality compared to non-lactic acidosis cases and higher serum lactate levels are associated with statistically significant mortality ($P = 0.04$) which is consistent with previous studies. High anion gap metabolic acidosis may be associated with higher mortality compared to normal anion gap acidosis as reported by Jung *et al.*,[5] whereas Cusack *et al.*[7] and Rocktaeschel *et al.*[8] reported no statistical significance in outcomes between these two groups. In our study, 31 patients had normal anion gap severe metabolic acidosis while 69 patients had high anion gap. There was no significance in the outcome between these two groups ($P = 0.540$). Jung *et al.*[5] and Kaplan and Kellum[9] reported that lower base excess is associated with high mortality. In our study, lower levels of base excess on admission are associated with statistically significant mortality compared to normal base excess levels ($P = 0.003$) which are consistent with previous studies.

This study focused on only single severe metabolic acidosis excluding mixed acidosis. Whether metabolic acidosis is an etiologic contributor to organ dysfunction or just a marker of severity of underlying illness has been a matter of debate. Of late, there are reports about severe metabolic acidosis playing a contributory role in organ dysfunction, decreased cardiac output, arterial dilatation and hypotension, arrhythmia, impaired oxygen delivery, increase in respiratory muscle workload, decrease in adenosine triphosphate generation, and altered immune response.[5]

The uncertainty over the timing and indications of bicarbonate buffer therapy and the controversy regarding the pros and cons of bicarbonate therapy was highlighted in an online survey by Kraut and Kurtz.[10] Gehlbach and Schmidt[11] reported high mortality after bicarbonate therapy and Stacpoole[12] reported higher mortality in lactic acidosis with bicarbonate therapy. Jung *et al.*[5] reported no significant outcome between patients who received bicarbonate therapy and patients who did not receive it. Bicarbonate therapy in acute high anion gap metabolic acidosis is controversial.[13,14] From the time of its conception, this study was never meant to assess the effect of sodium

bicarbonate on the outcome or to explore the reasons for sodium bicarbonate administration. However, the present study may be helpful as a primer to design a future interventional, randomized study to examine the effects of buffers in severely acidotic critically ill patients.

Limitations of this Study

- It was a prospective observational study. No intervention was done in this study.
- ABG analysis on the first day of admission was used for the study. No follow-up ABG analysis was taken into consideration.
- Lack of clear-cut guidelines for administration of bicarbonate buffer therapy.

CONCLUSION

This study highlights the magnitude of single severe metabolic acidosis on admission in critically ill patients admitted to ICUs under the Department of General Internal Medicine of JSS Hospital, Mysore, Karnataka, India. Severe metabolic acidosis in critically ill patients is associated with significant mortality. Higher serum lactate levels and base deficit, on admission, are excellent predictors of mortality. Patients with higher APACHE II score on admission had high mortality. Most common diagnosis in patients with severe metabolic acidosis in the present study is lactic acidosis. Most common diagnosis in patients with lactic acidosis in the present study is sepsis with septic shock. Most common diagnosis in patients with high anion non-lactic acidosis is diabetic ketoacidosis, whereas bicarbonate loss from GI tract (acute GE) is a common cause of normal anion gap acidosis. Early recognition of mortality predictors may improve the final outcome of the patient. Whether severe metabolic acidosis in critically ill is a significant abnormality in itself contributing to the causality of complications and mortality, which needs to be corrected, or is it just an association with underlying severe illnesses is difficult to ascertain.

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Review Article

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Comparative Advantage of the Novel Loop-Mediated Isothermal Amplification Technique over the Conventional Polymerase Chain Reaction

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Abstract

The role of gene amplification technology in the area of diagnostic medicine and other aspects of molecular biology has been very laudable. Molecular diagnostic has demystified the gray areas in disease diagnosis, making the process of disease management much easier and efficient. Several advancements in molecular diagnostics have been largely due to the introduction of the polymerase chain reaction (PCR). Hence, there is no doubt about the rank of the PCR, as one of the greatest molecular biological tools that existed in the last few decades. However, in this article we highlight the comparative advantages of a novel gene amplification technique called loop-mediated isothermal amplification (LAMP) over the conventional PCR. This innovative gene amplification technique has provided a solutions to the odds and limitations of the PCR through the unique features of the technique. The most interesting aspect of the LAMP, which is in contrast to the PCR is the affordability of the tool, hence, gives hope to the poor and resource-limited settings of the society. Other unique features of this novel technique are highlighted in this article.

Key words: Amplification, Diagnosis, DNA polymerase, Gene, Molecular diagnostic

INTRODUCTION

Accurate diagnosis is key in effectively treating, preventing, and achieving excellent prognosis. Over the last few decades, nucleic acid-based diagnostic techniques have tremendously improved disease diagnosis, limiting some of the challenges of disease diagnosis that previously existed. Despite the tremendous success recorded by the introduction of molecular diagnostic, widely credited to the use of polymerase chain reaction (PCR) there are still loop holes left to be filled. Development of a novel gene amplification technique called loop-mediated isothermal amplification (LAMP), has since gone to address those gray areas in molecular diagnostics. The LAMP is a unique nucleic acid amplification technique developed 14 years ago.[1] It has since been applied in numerous nucleic acid researches, and in clinical application as a screening tool.[2] It is a single tube technique that amplifies with high precision, few copies of DNA into billion copies within an hour.[1,3] It is a very rapid, sensitive, and efficient gene amplification technique.[1]

LAMP is increasingly gaining attention among researchers due to outstanding results obtained from numerous research work carried out with the technique (Table 1). It is an ideal tool for diseases diagnosis, with unique qualities which eliminate the odds of the PCR and other pre-existing molecular methods.[4] Techniques such as the nucleic acid sequence-based amplification, self-sustained sequence replication, strand displacement amplification, rolling circle amplification, and most prominently PCR are among the pre-existing molecular techniques.[5-9] These listed techniques have some common limiting factor which is well-addressed by LAMP. Most apparent is the relatively high cost of application, this has limits there use mostly to highly resourced facilities, like teaching hospitals, and

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Table 1: Pathogens of human and veterinary importance detected by LAMP

Target host	Pathogens (genome)	Classification of pathogen	References
Human	West nile virus	Virus(RNA)	[17]
Human	Japanese encephalitis virus	Virus (RNA)	[20]
Human	Norovirus	Virus (RNA)	[21]
Human	Dengue virus (1, 2, 3, and 4)	Virus (RNA)	[18]
Human	Avian influenza virus (H5N1)	Virus (RNA)	[22]
Human	HIV	Virus (RNA)	[23]
Human	BK virus	Virus (DNA)	[24]
Human	Rubella virus	Virus (DNA)	[25]
Human	Human papilloma virus (6, 11, 16, and 18)	Virus (DNA)	[26]
Human	Vericella-zoster virus	Virus (DNA)	[27]
Human	Adeno virus keratoconjunctivitis	Virus (DNA)	[28]
Human	Human herpes virus 6	Virus (DNA)	[29]
Avian	Newcastle disease virus	Virus (DNA)	[30]
Avian	Infectious bursal disease virus	Virus (RNA)	[31]
Avian	Mareks disease virus	Virus (DNA)	[32]
Avian	Infectious bronchitis virus	Virus (RNA)	[33]
Avian	Chicken infectious anemia virus	Virus (DNA)	[34]
Avian	Goose circo virus	Virus (DNA)	[35]
Canine	Canine parvo virus	Virus (DNA)	[36]
Equine	Equine Rota virus	Virus (DNA)	[37]
Caprine	Capripox virus	Virus (DNA)	[38]
Caprine	Capripox arthritis encephalitis virus	Virus (DNA)	[39]
Porcine	Porcine cico virus	Virus (DNA)	[40]
Porcine	Porcine cytomegalovirus	Virus (DNA)	[41]
Porcine	Classical swine fever virus	Virus (DNA)	[42]
Camel	Camel pox virus	Virus (DNA)	[43]
Human	*Vibrio cholarae*	Bacteria	[44]
Human	*Camplylobacter* spp.	Bacteria	[45]
Human	*Mycobacterium ulceran*	Bacteria	[46]
Human/animal	*Bacillus antracis*	Bacteria	[47]
Human/animal	*Listeria monocytogene*	Bacteria	[48]
Human/animal	*Escherichia coli*	Bacteria	[49]
Human/animal	*Staphylococcus aureus*	Bacteria	[50]
Human/animal	*Brucella* spp.	Bacteria	[51]
Porcine	*Yesrsiniaenterolitica*	Bacteria	[52]
Fish	*Vibrio alginolyticus*	Bacteria	[53]
Dog	*Anaplasmaphagocytophilum*	Rickettsia	[54]
Human	*Pneumocystis pneumonaea*	Fungi	[55]
Human	*Candida* spp	Fungi	[56]
Human	*Plasmodium falciparum*	Protozoan	[57,58]
Human	*Gardiaduodenalis*	Protozoan	[59]
Human	*Schistosmamansoni*	Protozoan	[60]
Human	*Leishmania* spp.	Protozoan	[61]
Human/animal	*Trypanosoma* spp.	Protozoan	[62]
Human	*Taenia* spp.	Tape worm	[63]
Ovine	*Theileria* spp.	Protzoan	[64]
Canine	*Babesiacanis*	Protozoan	[65]
Canine	*Echinococcusgranulosus*	Tape worm	[66]

LAMP: Loop-mediated isothermal amplification

in diagnostic centers found in countries with a robust economy.

STANDOUT PROPERTIES OF LAMP

LAMP employs four to six specially designed primers to hybridize six to eight distinct regions of a target gene. Hence gene amplification is done with high efficiency and precision.[1,3] In a LAMP reaction, all primers must have specific sequences to that of the target gene for amplification to commence, this strict principle of LAMP ensures high efficiency and reliability of the technique. LAMP uses a special polymerase enzyme called *Bst* DNA polymerase; this enzyme exhibits strand displacement activity as it extends annealed primer sequence.[10] This strand displacement activity is uniquely elicited by the LAMP polymerase enzyme without exonuclease activity at the 5'-3' as in the case of other strand displacement and isothermal nucleic acid amplification techniques.[1,11] Single-stranded DNA molecule can be obtained from this novel technique; this is achievable true the unique property of the *Bst* DNA polymerase.[11,12] Other standout properties of LAMP are enumerated below.

SIMPLICITY AND COST EFFECTIVENESS

The simplicity and cheapness of LAMP give room for its application both in resourced and resource-limited settings, the assay only requires a simple water bath or heat block, unlike the conventional PCR that requires a sophisticated instrument, such as thermo cycler, and the electrophoresis setup.[1,13] Although LAMP is a technically sound technique; however, it is simple to perform due to it straightforward principles, a semiskilled personnel can effectively perform the assay, and the protocols are highly comprehensive with no sophisticated instruments required. The reaction is rapidly and efficiently conducted in a single step. As illustrated in (Figure 1), LAMP result can be detected through visualization of turbidity resulting from accumulation of pyrophosphate ion released as byproduct in positive LAMP reaction.[11]

Real-time monitoring of LAMP can be accomplished, through spectrophotometric analysis using an inexpensive Real-time turbidimeter.[14] LAMP amplicon are quantified through Real-time monitoring of the amplification. The generation of a standard curve derived from plotting known concentration of gene copy number against time of positivity is followed to analyze the LAMP product.[2,14] Therefore, detection and quantification of LAMP product does not employ electrophoresis, which requires more time and extra working resources (Figures 1 and 2). Use of ethidium bromide in electrophoresis, a potential carcinogen is avoided. Mores on LAMP properties are listed in Table 2.

UNIQUE AND RAPID AMPLIFICATION

The ability of LAMP to amplify a target gene in a semi or unprocessed sample such as blood has taken the robustness of this technique to a greater level. The *Bst* DNA polymerase enzyme commonly used in LAMP has been demonstrated to be resistant to the presence of anticoagulants, hemin, N-acetylcysteine, Nacl, and other PCR-inhibiting substances.[15,16] Application of this property of LAMP will be beneficial in health care centers, where accurate and rapid diagnosis is most desired. The process will be much more rapid since the template extraction step has been omitted owing to this amazing property of LAMP.

EFFICIENCY

LAMP is a highly sensitive technique that amplifies few copies of template DNA in a reaction to a detectable level.[1] Forensic samples can be amplified with LAMP, as low as femtogram levels of DNA can be detected in a sample with few and degraded DNA copies.[4] It is considerably more sensitive than the PCR, the sensitivity of LAMP over PCR is evident in these studies, which

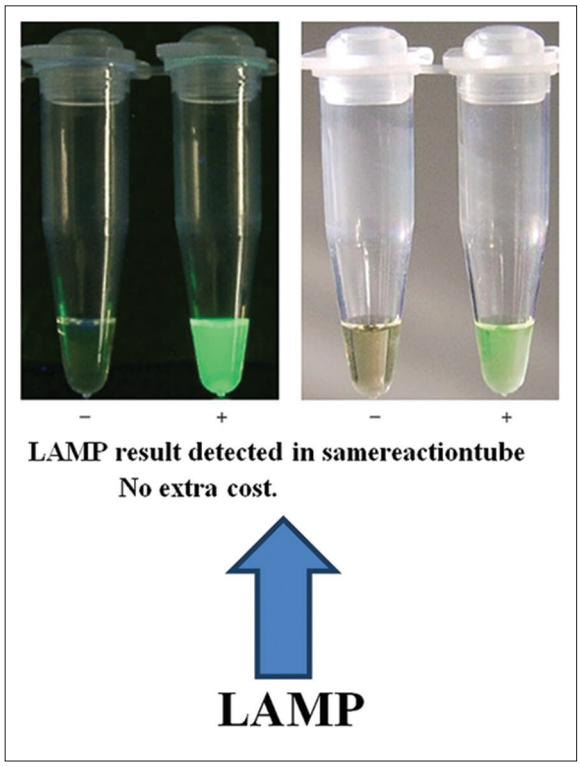

Figure 1: Amplification detection procedures (loop-mediated isothermal amplification)

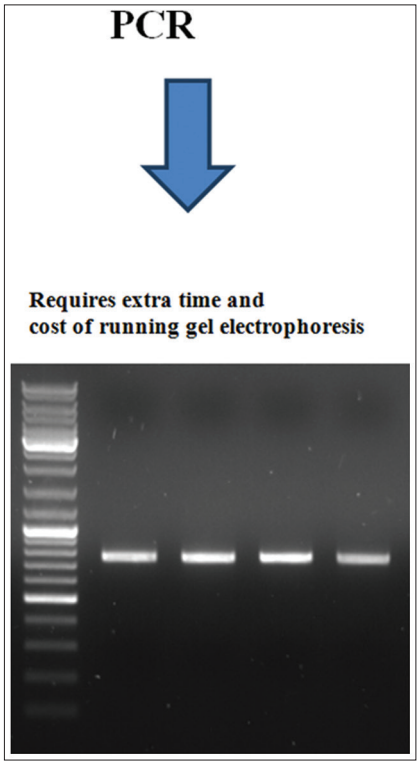

Figure 2: Amplification detection procedures (polymerase chain reaction)

Table 2: Comparative analysis of LAMP and PCR base on general principles of application

Property	PCR	LAMP	References
Amplification time	3-4 h	1 h	[1,3]
Specificity	High	Higher	[2,12]
Sensitivity	High	Higher	[18,19]
Simplicity	Sophisticated technique	Simple technique	[1,4]
Affordability	Expensive	Cheap	[1]
Accessibility of material	Readily available	Scarce	[2]
Purity of amplicon	Prone to carry over contaminations	Lower contamination risk due to closed tube system	[2]
Detection of result	By gel electrophoresis	Visual detection with naked eyes	[10]
Primers	Simple primer design (2 primers) involved	Complicated primer design (4-6 primers) involved	[2]
Stability	Inhibited by presence of impurities hence, only purely processed sample are amplified	Stable against sample impurities, can amply template DNA in a semi or unprocessed sample	[16]

LAMP: Loop-mediated isothermal amplification, PCR: Polymerase chain reaction

shows a 10-100 fold higher sensitivity than PCR with a detection limit of 0.01-10 Pfu of virus.[17,18] Accuracy of LAMP reaction is attributed to the nature of primers used.[3] Furthermore, high specificity of LAMP has been demonstrated through its ability to selectively amplify few copies of target DNA without interference of genomic DNA.[19] This remarkable specificity reflects on the strict adherence of four to six LAMP primers hybridizing to six or eight distinct regions of the target gene.[1-3]

Comparative Analysis of LAMP and PCR Base on Technique Essential Items and Protocols

PCR	LAMP
Thermocycler	Water bath or heat block
Thermo pol buffer	Thermo pol buffer
Taq polymerase enzyme	*Bst* DNA polymerase
DNA dye (optional)	DNA dye (optional)
Ethidium bromide	Not required
Electrophoresis setup	Not required

AMPLIFICATION PROTOCOL

PCR

The PCR amplifies DNA under three different temperature cycles, starting with the denaturation, followed by an annealing step and finally ends with the extension of the annealed primer sequence, annealing temperature varies according to the primer melting temperature (Tm), usually falls within the range below.

Denaturation ⟶ Annealing ⟶ Elongation

92°C-95°C 55°C-60°C 70°C-74°C

LAMP

Amplification begins and ends under the isothermal condition of about 60°C-65°C. The *Bst* DNA polymerase aids the annealing of outer primers to a double stranded template DNA, exhibiting its unique strand displacement activity.[1,12]

FUTURE PERSPECTIVE

Prompt and accurate disease diagnosis is a prerequisite for effective treatment and management of disease. The role of molecular diagnostic in health management is indispensable. The uniqueness of LAMP, which ranges from high stability, rapidity, simplicity, and cost effectiveness, has perhaps placed the novel technique above other molecular techniques. The high operational cost has been the most apparent limitation of PCR; LAMP promises to fill this gap limiting the use of PCR to only highly resourced settings. Several advancement has been made on LAMP since its advent, presently five versions of LAMP exist. They include the eLAMP, lyophilized LAMP, lateral flow assay LAMP, micro LAMP, and real-time monitoring and quantification LAMP. Pathologists and clinicians will benefit immensely from these advancements, due to the enhanced features introduced to the technology, making it more suitable in point of care diagnosis. Hence, continuous research is needed to fully explore and utilize the potentials of LAMP toward achieving a robust diagnostic tool. As enumerated in our previous review, unique principle of LAMP that made it very suitable can serve as a platform for improving on other techniques like the PCR.[67] The *Bst* DNA polymerase enzyme with strand displacement property is thought to be the most innovative features of LAMP.

CONCLUSION

The possible use of the powerful LAMP polymerase enzyme in PCR application will perhaps be a good area of research; this will no doubt lead to a major breakthrough in molecular diagnostic, by making the PCR much more simplified and cost-effective.

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Review Article

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New Therapy for Ocular Surface Disorders on the Horizon - Prosthetic Replacement of the Ocular Surface Ecosystem: A Review Article

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Abstract

Introduction: Prosthetic replacement of the ocular surface ecosystem (PROSE) has been a major innovation in the management of ocular surface disorders. It is a prosthetic device almost similar to a contact lens, designed for the purpose of daily wear. It creates a transparent, smooth optical surface over the damaged cornea. Furthermore, it has an expanded artificial tear reservoir that provides constant lubrication while maintaining the necessary oxygen supply. It has been proposed as management for ocular surface disorders against invasive procedure like keratoplasty. Several clinical studies have come forward with promising results. Limitations of PROSE include high cost and reduced access.

Key words: Cornea, Keratopathy, Keratoplasty, Lubrication, Prosthesis

INTRODUCTION

Prosthetic replacement of the ocular surface ecosystem (PROSE) is a novel treatment approach to ocular surface disease. It is a prosthetic device to replace and enhance the function of the ocular surface ecosystem, thereby improving vision, providing comfort and supporting ocular surface. PROSE was approved by the FDA in 1994 for daily wear in the treatment for irregular astigmatism and ocular surface disorders. Over the past 20 years, it has been referred as Boston scleral contact lens, Boston scleral lens, Boston scleral lens device, Boston scleral lens prosthetic device, and Boston ocular surface prosthesis (BOS-P).[1]

DESIGN

The prosthetic devices created by Boston Foundation for sight are transparent domes, almost size of a nickel. It is almost similar to a large hard contact lens and resembles in shape a margarita glass without the stem. PROSE devices fit under the eyelids, vaulting the damaged cornea, and resting on the sclera. Worn during waking hours, patients are trained in daily application, removal, and cleaning, as part of the treatment process (Figures 1 and 2).[1,2]

PROSE devices are made out of a highly gas-permeable hard plastic that allows oxygen to reach the cornea. They are designed to create a space between the prosthetic device and the eye that is filled with sterile saline. The liquid remains in the reservoir, providing constant lubrication by bathing the eye in a pool of artificial tears.[2]

Lack of corneal touch and positional stability excludes all sources of frictional micro trauma. The high oxygen permeability constant (Dk) of the material allows oxygen to diffuse readily through the lens matrix. PROSE treatment also overcomes the drawbacks of other modalities such as surgical risk and temporary effect of amniotic membrane grafting, the cosmetic and vision concerns of tarsorrhaphy, the contamination risk and the potential inconsistencies in preparation, and storage of autologous serum eye drops.[3]

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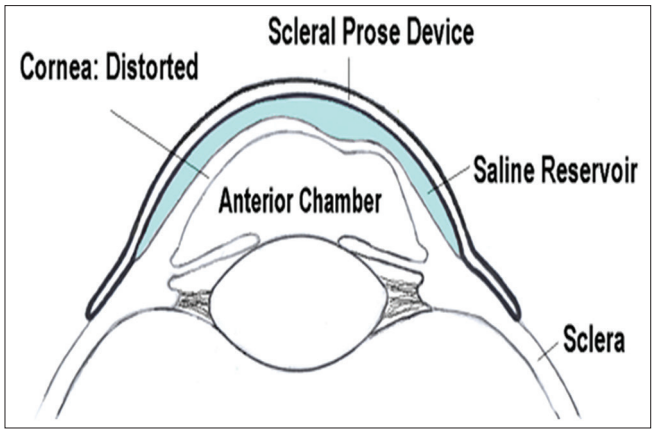

Figure 1: PROSE Device over a distorted cornea

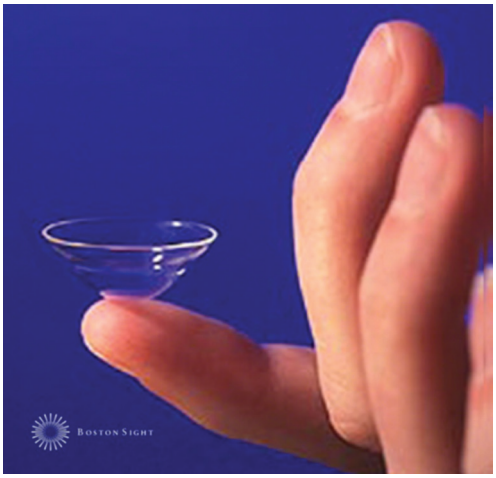

Figure 2: PROSE device

Prosthetic devices are customized by specially trained PROSE doctors and made on-site at the Boston Foundation for sight PROSE Manufacturing Lab.

PROSE CREATES

- A new clear, even optical surface over the irregular, damaged, or diseased cornea
- An artificial fluid reservoir that provides constant lubrication while maintaining the necessary oxygen supply.

INDICATIONS

1. Corneal ectasia: Eyes with advanced corneal ectasia can be successfully fitted with the PROSE device, and the Visual Acuity outcome was better and faster compared to keratoplasty.[4]
2. The most popular indication is for an ocular surface disease like persistent epithelial defect (PED). The mechanism by which PROSE supports re-epithelization in refractory persistent epithelial defect includes continuous lubrication, ocular surface protection, and maintenance of oxygenation.[3,5,6]
3. Steven Johnson Syndrome (SJS) and toxic epidermal necrolysis: with remarkable improvement in photophobia and surface breakdown, it also helps in healing of persistent epithelial defects associated with SJS when used on a daily wear basis.[5,7,8]
4. Limbal stem cell deficiency: Grover *et al.* report two patients with persistent epitheliopathy following treatment of conjunctival melanoma who were rehabilitated with PROSE. The authors finally concluded that "PROSE device can be a useful non-surgical option for these patients."[5,9]
5. Neurotrophic keratopathy: Gumus *et al.* published a case report on the use of PROSE device in the management of persistent corneal epithelial defect from herpes zoster ophthalmicus. Along with other modalities of treatment such as oral doxycycline, autologous plasma, punctal plugs, multiple therapeutic lenses, and double layer amniotic membrane transplantation, he combined PROSE therapy. A remarkable change in the epithelial defect was seen within 3 weeks of daily use.[5,10]
6. Atopic keratoconjunctivitis - PROSE device can be considered in these patients with PED, who are poor candidates for contact lens use. It promotes rapid healing of PED.[5]
7. As a pharmaceutical reservoir - With PROSE, fluid turnover is low, allowing for prolonged availability of drugs in the reservoir. Epithelial toxicity could be enhanced by sustained contact. Hence, care is taken to use only preservative-free solutions.[3]

TREATMENT PROVIDERS

PROSE treatment is provided by a group that is inclusive of an ophthalmologist (Cornea Specialist), optometrists who have completed the PROSE Fellowship and ophthalmic technicians.

Treatment takes almost 4-12 day long visits to complete, with periodic follow-up visits as needed during the first 6 months.

CUSTOMIZATION PROCESS

PROSE doctors customize multiple trial prosthetic devices. Each step is followed by a trial session to make sure each patient achieves the best fit possible. The final device is unique to each patient's eye condition.

PATIENT TRAINING

Patients participate in three or more training sessions to learn application, removal, and care of their prosthetic devices. Family members and caregivers are also trained to assist patients.

FOLLOW-UP WITH PRIMARY EYE CARE DOCTOR

Patients are asked to follow-up with their referring ophthalmologist within 2-3 weeks of finishing treatment. Meanwhile, ongoing care is provided by the primary eye care doctor in co-ordination with the PROSE treatment providers.

ANNUAL EVALUATION

Patients are advised to come for Annual follow-up to their PROSE provider for a detailed evaluation of their PROSE devices, make adjustments as required and address any related issues.

Figure 3: Plunger

Figure 4: Method of insertion

ACCORDING TO THE BOSTON FOUNDATION FOR SIGHT

Following are the requirements for insertion:

a. An application plunger
b. A removal plunger
c. Two alcohol wipes
d. A small mirror
e. Preservative-free saline (Figures 3 and 4).

CARE AND HANDLING OF THE PROSE DEVICE

Following are the requirements:

- One PROSE disinfection case
- One unopened package of Clear Care™ (Figures 5 and 6).

Figure 5: Disinfection case

Figure 6: Prosthetic replacement of the ocular surface ecosystem cleaning solution

CENTERS IN INDIA PROVIDING PROSE TREATMENT[2]

1. LV Prasad Eye Institute, Hyderabad
2. Sankara Nethralaya, Chennai
3. The eye super Specialities, Mumbai.

LIMITATIONS

Limitations to the wider adoption of PROSE treatment include cost and availability at a limited number of tertiary eye care centers. An economic appraisal found that PROSE treatment is cost effective and cost beneficial in patients with severely compromised visual function attributable to the ocular surface disease. Others have also reported that epithelial defects that required PROSE for healing and typically recur following cessation of therapy. In comparison to earlier series of cases, the rate of microbial keratitis as a complication of treatment has been reduced by the use of a non-preserved topical fourth-generation fluoroquinolone in the device reservoir.[3]

CONCLUSION

PROSE could be considered as a treatment option against an invasive procedure like keratoplasty for many ocular surface disorders. Numerous research articles are supportive of the same. Many ongoing research works are also happening to prove the benefits of PROSE over keratoplasty.

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Case Report

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Synovial Cell Sarcoma Arising from Pleural Cavity: A Rare Case Report

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Abstract

Synovial cell sarcoma is the third most common case of soft tissue sarcoma in adolescent and young adult age group. Synovial sarcomas are rare malignant neoplasms of unknown histogenesis, most common affecting the lower extremities and frequently arises adjacent to joints or tendon sheaths. Synovial sarcoma is a misnomer because the tumor does not arise from the synovium; it only resembles synovial tissue at light microscopy. Since it appears to arise from as yet unknown multipotent, stem cells that are capable of differentiating into mesenchymal and/or epithelial structures and lack synovial differentiation. Synovial cell sarcoma arising from the pleural cavity is very rare in incidence and even rarely documented in literature. We here present a case of synovial cell sarcoma in a 25-year-old male arising in the pleural cavity.

Key words: Pleural cavity, Soft tissue sarcoma, Synovial cell sarcoma

INTRODUCTION

The name synovial cell sarcoma is a misnomer. The origin of synovial cell sarcoma is unclear. The name synovial cell sarcoma is given because of similarity between tumor cells and synoviocyte. Extremities is the most common site but a part from the extremities; synovial sarcoma may arise within head and neck, esophagus, retroperitoneum, and also in the thorax; mediastinum, heart, lung, pleura, or pericardium with lesser frequency.[1,2] It preferentially affects young individuals.[3] Recent data suggest the neurological origin of synovial cell sarcoma.[4] Chromosomal translocation in synovial cell sarcoma is t(X;18)(p11;q11).[5] Due to the fusion of gene SYT on chromosome 18 with gene SSX on chromosome X. Synovial cell sarcoma usually presents as a some nodule over extremities which remains benign for long duration and then increases rapidly in size. Prognosis of synovial cell sarcoma-like another soft tissue sarcoma is very poor. Surgical resection should be performed, whenever possible with neoadjuvant chemotherapy.

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CASE REPORT

A 25-year-old male presented to outpatient department with complaint of left sided chest pain since 1 month and dyspnea on exertion since 1 month. There was no significant past history. On examination, breath sound was decreased on left infraxillary, inter- and infrascapular area. Chest X-ray posteroanterior view (Figure 1) and left lateral view (Figure 2) were suggestive of homogenous opacity occupying left lower zone with blunting of left costophrenic angle and cardiophrenic angle. Ultrasound chest revealed a pleural based mass. Computed tomography (CT) chest showed – A mass lesion arising from pleura and occupying the lower half of left hemithorax (Figure 3). CT guided biopsy was done which showed – spindle-shaped ells arranged in interlacing fascicles with intervening collagenous bundles (Figure 4). Cells have nucleus oval to elongated nuclie with moderate cytoplasm and indistinct cell borders. Immunohistochemical study was positive for smooth muscle actin (SMA), epithelial membrane antigen (EMA)

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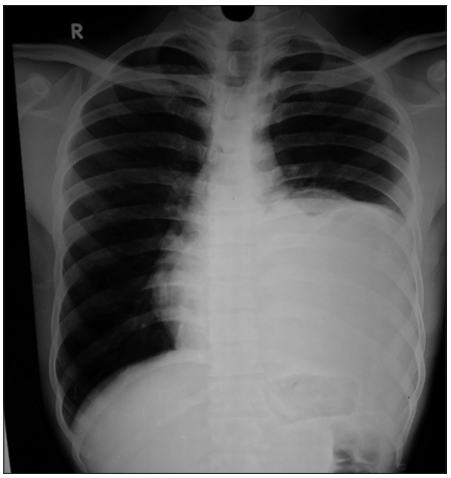

Figure 1: Chest X-ray postero-anterior view showing homogenous opacity in left lower zone blunting left cardio- and costophrenic angle

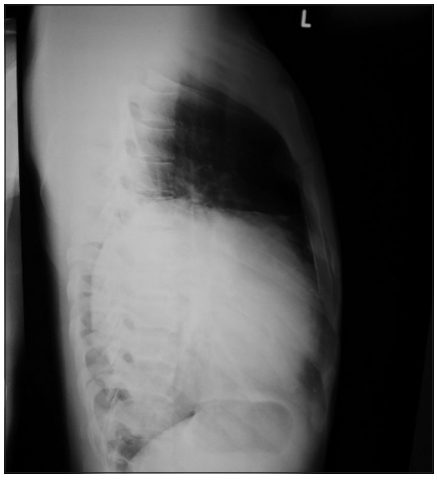

Figure 2: Chest X-ray left lateral showing a mass lesion in left lower lobe

and Bcl2. A diagnosis of synovial cell sarcoma was made based on biopsy and immunohistochemistry report.

DISCUSSION

Synovial cell sarcoma is very rare tumor arising from immature mesenchymal cells. Pulmonary sarcoma comprises around 0.5% of lung malignancies. Chest pain, cough, hemoptysis are the common presenting complaints. The usual age of presentation is 25-30 years. Synovial cell sarcoma as often misdiagnosed as solitary fibroma, malignant fibrous histocytoma due to rarety of its incidence. Histology along with immunohistochemistry studies are diagnostic. Immunohistochemically, synovial sarcomas are nearly uniformly positive for cytokeratin, EMA, bcl-2, and vimentin, and negative for S-100, desmin, SMA, and vascular tumor markers. prognosis is very poor with 5 years survival rate of <50%.[6] Synovial sarcomas are

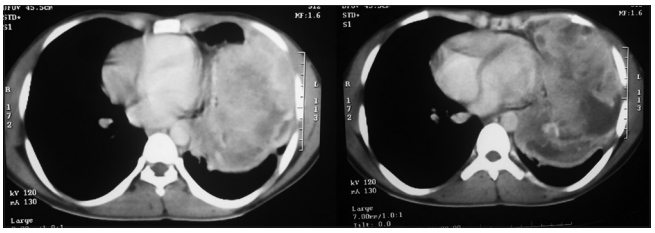

Figure 3: Contrast enhanced computed tomography chest showing mass lesion with contrast enhancement with areas of necrosis

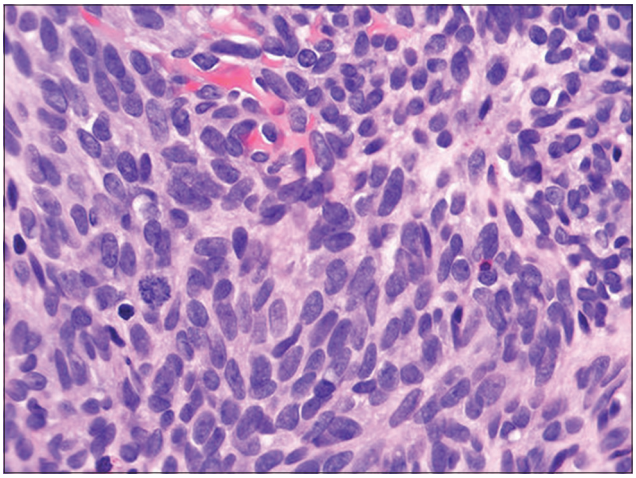

Figure 4: Pathology appearance of synovial cell of sarcoma

chemosensitive to ifosfamide and doxorubicin, however, the response rate is only 24%.

CONCLUSION

This case is one of the few case reports of primary pleural synovial sarcoma described in literature. It is often misdiagnosed as tuberculosis especially Indian subcontinent, which delays the diagnosis. Owing to its rarity and the paucity of data regarding its natural history, there are no guidelines for optimal treatment. Meanwhile, it consists of surgical resection associated with chemotherapy and/or radiotherapy. In our case, arriving at the correct diagnosis, with contemporary interventional pulmonology methods, and chemotherapy has improved the outcome of this otherwise aggressive tumor.

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Case Report

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Management of Acardiac Twins: Does Conservative Approach Deserves Consideration? A Case Report

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Abstract

Acardiac twinning, a rare congenital anomaly of monozygotic twin pregnancies, often leading to abnormal placental vascular anastomosis. This in turn results in twin reversed arterial perfusion (TRAP) with complex pathophysiology. Current information on early diagnosis and treatment for the salvation of the pump twin is based mainly on various individual case reports. Here, we report a case of monozygotic twin complicated with TRAP sequence, which was diagnosed early, managed conservatively and the outcome was excellent. With the availability of various sophisticated studies for antepartum fetal surveillance, outcomes in expectantly managed cases are getting better. So, in acardiac twins aggressive interventions should be used cautiously and should be reserved only for some really indicated cases.

Key words: Acardiac twin, Conservative management, Monochorionic twins, Twin pregnancy, Twin reversed arterial perfusion sequence

INTRODUCTION

Acardiac malformation also known as twin reversed arterial perfusion (TRAP) sequence, is a unique complication of monochorionic pregnancies. It is characterized by paradoxical retrograde perfusion of abnormal twin by structurally normal pump twin through a single artery-artery anastomosis.[1] It is a very rare condition. The reported incidence being 1 in 35,000 deliveries and 1 in 100 monozygotic twins.

Optimal management of acardiac twin pregnancies is controversial. The reported fetal/neonatal mortality of the pump twin is extremely high (50-60%). It is thought primarily to be due to increasing in cardiac demands of the pump twin in an effort to perfuse its acardiac sibling. Data suggest 50% mortality rate in pump twin with expectant management.

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CASE REPORT

A 25-year-old G2P1L1 with previous cesarean section done referred to our tertiary care center at 10 weeks of gestation as a case of monochorionic and monoamniotic (MCMA) twins with single fetal demise. She had excellent dates. Her family history and past history were absolutely unremarkable for twins or perinatal issues. All routine investigations were done and found to be within normal limits. Since then the patient had regular antenatal check-ups from our institute. During routine antenatal care at 20 weeks of gestation, the abdomen was enlarged to around 24 weeks. We got an ultrasound (USG) scan done. To our surprise, USG revealed a twin pregnancy with a single placental mass, and there was no dividing membrane (MCMA). There was appropriate for dates twin without any obvious anomalies, which was associated with an acardiac, acranial amorphous twin (Figure 1). At that time size of the cardiac twin was almost same as the pump twin. But, pump twin showed no signs of decompensation. We discussed in detail with parents about the condition, and we also counseled them about the risks and benefits of the expectant management and surgical intervention.

Management and Outcome

Pregnancy was followed up carefully with serial USG studies, Doppler flow studies, non-stress test (NST),

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biophysical profile (BPP), and fetal echocardiography. USG with Doppler study was done once in 2 weeks. Echocardiography was done at 24, 28, and 32 weeks of gestation. We looked closely for the presence of any signs of decompensation like pericardial or pleural effusion, or ascites. Serial USG scan revealed that acardiac twin was constantly increasing in size. USG at 32 weeks of gestation showed the acardius which had increased in size relative to the pump twin, who had maintained an appropriate weight for gestational age with an estimated fetal weight of 1.960 kg. But, pump twin showed no signs of decompensation. The patient was admitted at 30 weeks of gestation. Alternate day NST was done, which was found to be reactive. Two doses of betamethasone were given 24 h apart for fetal lung maturity.

At 34 weeks of gestation, the patient presented with preterm premature rupture of membranes. Emergency lower segment Cesarean section was done. Pump twin weighed 1.9 kg with APGAR 1'9. Acardiac twin weighed 2.9 kg, its head, and upper extremities were absent. It had well-developed lower limbs (Figure 2). Pump twin was apparently alright, and it showed no apparent anomalies (Figure 3). The baby was kept in NICU for 12 h for observation. As there were no signs of failure, it was managed on mother side only.

Postnatally pump twin was healthy. Both mother and baby were discharged on day 6.

DISCUSSION

Acardiac twinning or TRAP sequence is a rare congenital anomaly of monozygotic multiple pregnancy. This occurs secondary to abnormal placental anastomosis which is characterized by formation of a malformed fetus with an absent or rudimentary heart (acardius) and other structures.[1]

The pathogenesis in TRAP sequence is, there will be a defect in embryogenesis in one of the twin leads to failure of cardiac development. The normal twin then perfuses the acardiac twin via placental artery-artery anastomoses.[2] It should be noted that the cardiac anomaly is not secondary to anastomoses, but they are established as a result of it.[3,4]

Within the placenta, which is singe and shared by both the twins, arterial perfusion pressure of the donor twin exceeds that of the acardiac twin who thus receives reverse blood flow of deoxygenated arterial blood. This used blood reaches the recipient twin through its umbilical arteries, and it preferentially goes to iliac blood vessels. Thus, only the lower extremity is perfused and disrupted growth and development of the upper extremity results as occurred in the present case.[5]

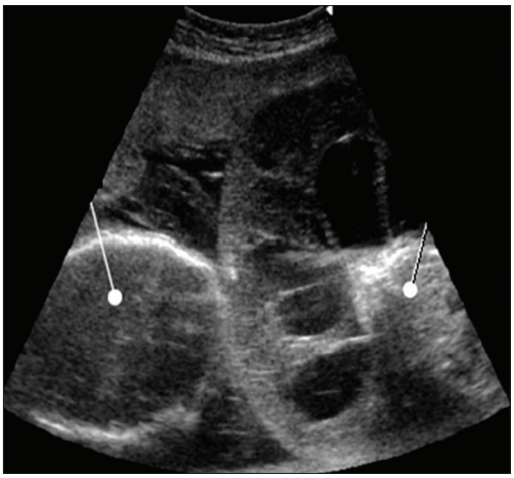

Figure 1: Ultrasound taken at 20 weeks of gestation showing pump twin and acardiac twin.

Figure 2: Acardiac twin

Figure 3: Pump twin

The main differential diagnosis of acardiac twin is the intrauterine death of one of the monochorionic twin, which

will be anomalous. (In the present case, it was misdiagnosed in 10 weeks USG as MCMA twin with single fetal demise). However, the continued growth of the "presumed dead" twin on subsequent scans is often the first clue to the correct diagnosis. The color flow imaging plays a major role in establishing the diagnosis of acardiac twin. This shows the presence of blood flow within the abnormal fetus. This may be evident even during the first trimester.[6]

When blood flow pattern is examined in detail in these cases, it reveals a paradoxical direction of arterial blood flow toward acardiac twin. Lately, three-dimensional USG has also been used for confirmation of diagnosis and also to establish the extent of fetal malformation.[7]

It is clear that TRAP sequence poses substantial risks for the pump twin. Ideally, a diagnostic test would allow us to distinguish between cases that can be safely managed expectantly and those that require intervention. USG with Doppler studies, BPP, NST, and fetal echocardiography play a significant role in deciding the course of treatment.

Even though the pathophysiology of acardiac twin has been clearly resolved and treatment by ablating this vascular connection has been proposed, the availability and difficulty of this mode of treatment and fetal death secondary to the treatment itself have been clearly demonstrated. Invasive treatment should be restricted, only to those pregnancies which would benefit from prenatal intervention like those where the donor twin is at a significant risk of prematurity, cardiac failure or death and should be considered in presence of poor prognostic factors such as polyhydramnios, ascites, large acardiac twin, and rapid growth or evidence of substantial blood flow through the umbilical vessel supplying the acardiac twin.[8]

Sullivan *et al*. advocated expectant management in all cases complicated with TRAP sequence.[9] 90% survival in pump twin were reported in 10 pregnancies with an acardiac twin managed expectantly. They recommended expectant management with close fetal surveillance in all cases, and aggressive interventions should be used cautiously.

The best time to intervene and best mode of intervention are not yet known. With an increase in antenatal diagnosis and with the availability of various sophisticated studies for antepartum fetal surveillance, outcomes in expectantly managed cases are getting better, and they are better than reported.

In the presented case, even though pump twin weighed only 3/4th the weight of acardiac twin it showed no signs of decompensation. The outcome, in this case, was excellent.

CONCLUSION

The most appropriate interventions and management protocols for the various clinical presentations of TRAP Sequence is as yet to be determined, and conservative non-intervention is often appropriate in some carefully selected cases. This case report demonstrates that in TRAP sequence, early diagnosis, close antenatal follow-up can prevent unnecessary interventions without compromising the outcome. Long-term follow-up data on surviving pump twin are lacking. It is anticipated that centers with active study protocols for these conditions will best serve patient care and clinical research needs.

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Case Report

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Lumbar Hernia: A Case Report and Review of Literature

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Abstract

Lumbar hernias are among the rare hernias. They need high clinical suspicion as their signs and symptoms are usually non-specific. Patients are usually 50-70 years old. They commonly affect males and frequent on the left side. Here, we describe a 61 years male patient presented with left side primary inferior lumbar hernia which was supported by magnetic resonance imaging of abdomen and pelvis. They should be repaired as soon as possible to avoid complication. Here, he was undergone laparoscopic surgery with mesh hernioplasty. He resumed his routine activities within 2 weeks. After 1 year follow-up, he is alright without any symptoms or signs of recurrence.

Key words: Hernioplasty, Lumbar hernia, Laparoscopy

INTRODUCTION

Lumbar hernia is a rare entity with only fewer than 310 cases reported so far in the world.[1,2] It account for <1.5% of all abdominal hernias. Congenital hernias are usually small in size at the time of presentation; most commonly occur through the inferior lumbar triangle. Usually, clinical diagnosis is difficult due to non-specific symptoms.[3] They are prone to incarceration and strangulation, so surgery is advisable as soon as possible.[4,5] Primary acquired variety occur spontaneously, whereas secondary acquired variety occurs due to trauma, infection, or surgical incisions.[6] Surgical methods should be planned on the basis of etiology and hernia size.[7]

CASE REPORT

A 61 years male presented with pain and swelling in the left lumbar region since 6 months. He was a known case of hypertension under medication. All systemic examination are within normal limits. On examination, a single oval swelling of size 6 cm × 4 cm arising from the left inferior lumbar triangle found, which impulse on coughing, non-tender and reduces with a gurgle, on auscultation bowel sound heard. Abdominal muscle tone was good, and other hernial orifices were normal. Ultrasonography revealed a breach in peritoneum at the left lumbar region of size 5.3 cm × 3.4 cm with herniation of omental fat. Magnetic resonance imaging showed a wide neck left side inferior lumbar hernia containing descending colon and extraperitoneal fat (Figure 1). After controlling

Figure 1: Magnetic resonance imaging showing left side inferior lumbar hernia containing descending colon and extraperitoneal fat

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hypertension, the patient was posted for laparoscopy pre-peritoneal onlay mesh hernioplasty with prolene mesh (Figure 2). With the patient positioned in a 45° left semi-lateral position, the peritoneum is incised above the hernia (Figure 3) and dissected back to expose the muscle defect (Figure 4). The contents are reduced and a prolene mesh fixed to the 12th rib superiorly, iliac crest inferiorly, erector spinae fascia medially, and external oblique fascia laterally (Figure 5). Splenic flexure of the colon and retro-peritoneal fat were the content. The peritoneum then resutured to cover the mesh. His post-operative recovery was uneventful. He discharged on the 3rd post-operative day and resumed his routine activities within 2 weeks. After 1 year of follow-up, he is alright without any symptoms or signs of recurrence.

DISCUSSION

Barbette, in 1672, first suggested the existence of a lumbar hernia.[8] Garangeot reported the first incarcerated lumbar hernia in 1731. Grynfeltt and Lesshaft independently described superior lumbar hernias in 1866 and 1870, respectively.[9,10] Jean-Louis Petit first described inferior lumbar triangle in 1738.[11] Lumbar hernia is one of the rare hernias, so most surgeons are not exposed to. Hence, delayed diagnosis and delay in treatment, causing increased complication and increased morbidity.[3] It occurs more common in males (3:1) and is more frequent on the left side than the right (2:1).[12] They are classified into congenital (20%) and acquired (80%). Again acquired variety is divided into primary or secondary. Primary acquired hernias occur spontaneously and being the most common (55%). Secondary acquired hernias constitute about 25% of all lumbar hernias.[13] Like other hernias, they gradually increase in size. They are prone to incarceration and strangulation, so surgery is advisable as soon as possible.[4,5] Herniorrhapy is difficult, so hernioplasty is recommended. As for every hernia, it is important to create a tension-free mesh repair.

Most primary lumbar hernias occur through the inferior lumbar triangle of petit and less commonly through the

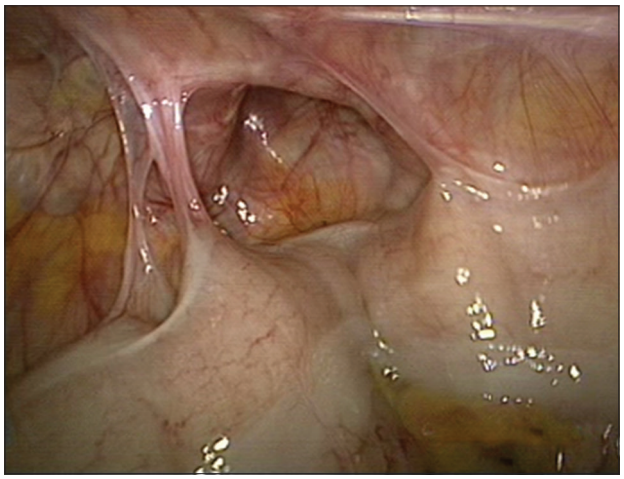

Figure 2: Trans-abdominal laparoscopic view showing the hernia defect and adhered descending colon

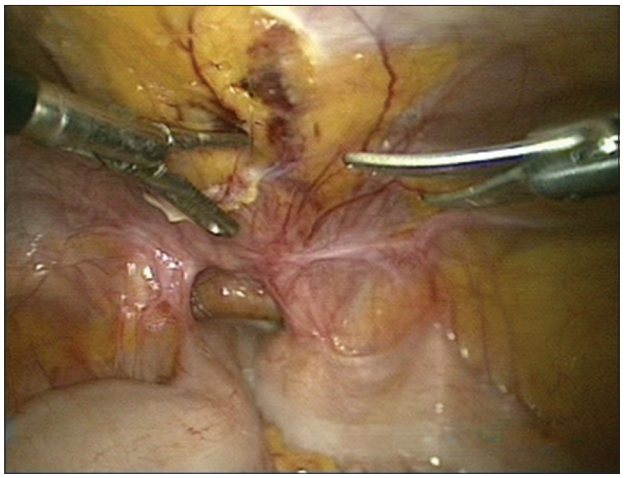

Figure 3: Incision of peritoneum above the hernia defect

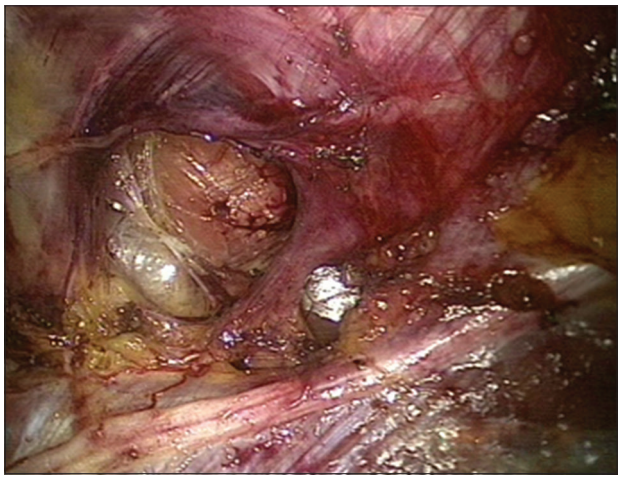

Figure 4: Exposed muscle defect after completion of the dissection

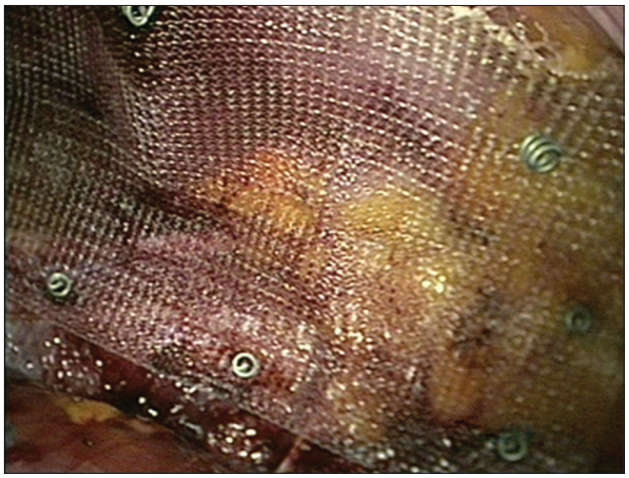

Figure 5: Tension-free prolene mesh placement over the defect

superior lumbar triangle of Grynfeltt.[8] A lumbar hernia must be distinguished from a lipoma, a cold abscess pointing to this position and pseudo-hernia due to local muscular paralysis.

Burick and Parascandola first introduced the trans-abdominal laparoscopic approach for lumbar hernia repair.[14] Laparoscopic repair has the advantage of less pain, shortened hospital stay, good cosmetic, and functional results.[15] For recurrent or large defects (especially if there is a component of neuropathic muscle atrophy present), anterior repair approach is preferable as a double mesh or a gluteus aponeurosis flap are needed.[16,17] Other methods can be used, e.g., mesh plug or retroperitoneoscopic tension-free mesh repair.[18-20] Post surgery seroma formation is common but resolves spontaneously, hardly need an aspiration of the fluid.

CONCLUSION

The choice of surgical procedure for the lumbar hernia should be individualized according to the etiology and size of the defect. And whenever possible, laparoscopic hernia repair should be taken priority over open procedures.

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Case Report

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Incidentaloma

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Abstract

An incidentaloma is a benign tumor found coincidentally without relevant clinical symptoms or suspicion, diagnosis of which has increased with increased use of modern imaging technology becoming a common management scenario. Incidentaloma (Conns' syndrome) is a disease of the adrenal glands involving the excess production of aldosterone and patient usually presents with clinical features of hypokalemia and hypertension. Atypical clinical presentations with a combination of normotension and normokalemia are described in few cases. In this case report, the patient presented with a headache, abdominal pain, and essential hypertension only. To rule out other pathology ultrasonography was performed and underlying adrenal adenoma was found. Vigorous control of blood pressure using adequate antihypertensive medications subsequently lead to symptomatic relief.

Key words: Adrenal adenoma, Essential hypertension, Normokalemia, Primary hyperaldosteronism, Ultrasonography

INTRODUCTION

The finding of adrenal incidentalomas (AI) is reported to be as high as 8% and 4% in autopsy series and radiologic series, respectively.[1,2] Primary hyperaldosteronism (HA) is the most common form of endocrine hypertension and is now considered as the most common cause of secondary hypertension.[3] It usually presents with features of hypokalemia such as muscle cramps, weakness, tetany, and severe or resistant arterial hypertension. However, there is a varied spectrum of presentation with clinical and biochemical variations in primary HA. In particular, hypokalemia is not evident in up to one-third of cases, and normotensive primary HA is rare.[4,5] Other than these variations, primary HA rarely presents in an emergency room with a catastrophic complaint constituting a diagnostic dilemma.[6] The consideration of size and radiographic appearance of the mass are of particular importance. Suspicious adrenal masses of ≥4 cm are advised surgical removal. Masses <4 cm if found to be hormonally active, should also be removed but usually recommended for observation for an increase in size.[7]

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CASE REPORT

A 70-year-old female arrived in the Medicine Department with a recurrent headache since 2 years associated with myalgia, backache, history of on and off abdominal pain, and bilateral swelling on legs. History of hypertension was recorded on a couple of occasions during past 2 years, but no treatment of hypertension was prescribed and advised follow-up. There was no history of thyroid illness, connective tissue disease, and similar complaints. The patient had undergone hysterectomy and cholecystectomy 21 and 10 years back, respectively. Clinical examination revealed that it is a case of hypertension with pitting edema and no palpable abdominal mass. Neurological examination revealed full strength in all muscles with normal deep tendon jerks. The patient was under observation for blood pressure monitoring, and it was recorded a maximum of 164/90 mm of Hg and a minimum of 146/80 mm of Hg without any use of antihypertensive drugs. Serum electrolytes reports of sodium, potassium, and chloride were 134, 4, and 92 meq/L, respectively. Thyroid function tests, urine routine microscopy, and renal function tests were normal. Electrocardiography showed left bundle branch block without changes of hypertension or hypokalemia

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(Figure 1). Ultrasonography (USG) of the abdomen showed a 2.3 cm × 1.3 cm hypoechoic, round lesion in the left adrenal gland. Computed tomography scan abdomen confirmed the left adrenal adenoma with nonhomogenous enhancement (Figure 2). Plasma renin activity (PRA) was 2.0 ng/mL/h, and plasma aldosterone was 405.4 pg/mL. Overnight dexamethasone test revealed suppressible cortisol levels. 24 h urinary vanilmandelic acid measured 1.12 mg/24 h. Various biochemical markers measured with optimum precautions, their levels are adrenocorticotropic hormone 25 pg/ml, adrenaline 1.52 pg/ml, noradrenaline 1.42 pg/ml, and cortisol 109 ng/ml. Diagnosis of Conns' syndrome was established by hypertension, raised plasma aldosterone, decreased PRA, and adrenal adenoma on magnetic resonance imaging.

Management

The patient was prescribed a combination of the antihypertensive medications angiotensin receptor blocker and diuretic (telmisartan and hydrochlorothiazide, 40/12.5 mg). The reduction in blood pressure lead to a subsequent headache relief within 7 days. The patient has been advised a routine USG every 6 months to check progression of the tumor for further management of disease.[8]

DISCUSSION

Patients suspected to have primary HA used measures the plasma aldosterone concentration (PAC) to PRA ratio as the first investigation to support a suspicion of the disease. A high ratio of PAC to PRA (202.73), i.e., >25 signifies HA if the aldosterone concentration is >15 ng/dL.[9] HA should be screened for in every hypertensive patient with AI. Traditionally, HA has been clinically associated with hypokalemia and hypertension. However, normokalemia occurs in up to 50% of patients with HA.[10] Thus, hypokalemia is not a useful marker for the purpose of screening. The best screening test is upright PAC to plasma aldosterone renin ratio. Primary HA is now increasingly being recognized as the underlying cause in patients suffering with essential hypertension.[11]

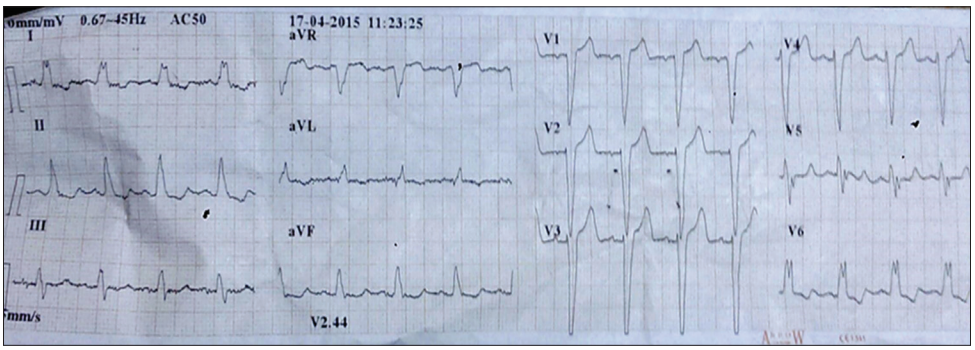

Figure 1: Electrocardiography showing left bundle branch block but no U waves of hypokalemia

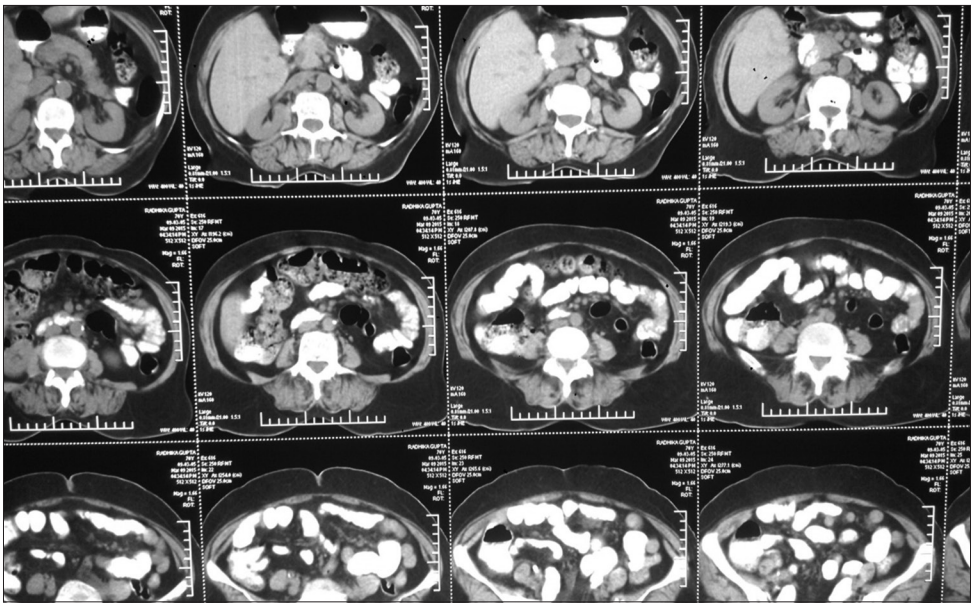

Figure 2: Computed tomography scan abdomen showing left adrenal adenoma

The likelihood of primary HA seems directly related to the severity of hypertension with increased incidence in patients with severe hypertension and lesser (<2%) with mild hypertension. An initial increase in sodium reabsorption related to the effect of aldosterone on distal renal tubules explains the arterial hypertension of primary HA. Aldosterone effect on the central nervous system, increased peripheral vascular resistance and increased vascular sensitivity to vasopressors such as angiotensin and adrenalin are factors responsible for higher blood pressure. The occurrence of normal blood pressure in primary HA is rare; in case of middle-aged females, the diagnosis is usually raised by clinical features of hypokalemia (fatigue, paresthesia, and tetany).

CONCLUSION

The varying clinical presentations of primary HA present a diagnostic dilemma to the clinicians. The usual approach of hypertension with hypokalemia to suspect this condition may be missing in many borderline hypertensive and normotensive cases. Atypical presentations are increasingly being described. All cases of hypertension must be screened for this condition.

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Case Report

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Nodular Hidradenoma: A Cytohistological Correlation on Fine-Needle Aspiration Cytology

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Abstract

Cytodiagnosis of adnexal tumors is challenging by virtue of an enormous number of individual tumors and their variant forms. We report a case of nodular hidradenoma in a male patient aged 59 years who presented with nodular swelling at the outer canthus of the left eye. Clear cell hidradenomas arise as nodules from eccrine sweat glands. It is an uncommon benign adnexal neoplasm that is more common in adults than in children. The diagnosis is usually based on histopathology, and the lesion is rarely diagnosed on fine-needle aspiration cytology (FNAC), hence merits mention. Overall our study established that the FNAC can be used as the first line of diagnostic investigation for most of the nodular lesions of the skin.

Key words: Adnexae, Basaloid, Eccrine, Hidradenoma, Nodular

INTRODUCTION

Nodular hidradenoma is a cutaneous neoplasm that may appear at various sites all over the body. It is common been referred as clear cell hidradenoma or sweat gland adenoma[1] of eccrine origin. Nodular hidradenomas arises as intradermal from eccrine sweat glands as intradermal nodules. Electron microscopic ultrastructural features and histochemical enzyme analysis have shown nodular hidradenomas to be an intermediate entity between eccrine poroma and eccrine spiradenoma.[2] The histology of the malignant hidradenoma resembles that of its benign counterpart. The criteria for malignancy includes poor circumscription, the presence of nuclear atypia, along with presence of predominantly solid cell islands, infiltrative growth pattern, necrosis, mitotic activity, and angio-lymphatic permeation.[3-5] Sweat gland tumors of the eyelid are quite rare yet the possibility of sweat gland tumors has to be considered during differential diagnosis of eyelid tumors. The malignant forms are even more unusual in appearance. We report a case of malignant nodular hidradenoma in a 59-year-old man, who presented to the outpatient department with a nodular swelling in the outer canthus of the left eye.

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CASE REPORT

The 59-year-old man presented with enlarged, painless nodular mass in the outer canthus of the left eye that began 4 years prior with a rapid increase in size over the last 3 months. Additional complaints of pain, ulceration, and bleeding were also associated. Physical examination revealed a solitary pigmented nodule on the outer canthus measuring 1.5 cm × 0.5 cm, fleshy with central ulceration. The nodule was firm to hard in consistency. There was no regional auricular, cervical, or submandibular lymphadenopathy. Hematological investigations and biochemical parameters were within the normal limit. Clinical provisional diagnosis of basal cell carcinoma and squamous cell carcinoma is given, and the patient sent to cytology department for fine-needle aspiration cytology (FNAC).

Microscopy

May-Grunwald-Giemsa stain (Figure 1) and hematoxylin and eosin stain (Figure 2) revealed high cellularity comprising of numerous large sheets of cells with papillary fronds and overcrowding of cohesive three-dimensional groups of monomorphic cells. Occasional duct, like

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tubular structures, is also seen. Cells are polygonal with a round to ovoid nuclei, smooth nuclear contour, dense nuclear chromatin, inconspicuous nucleoli with abundant cytoplasm. Some cells showed very scanty cytoplasm thereby imparting a basaloid appearance resembling myoepithelial cells. Few squamoid to spindly cells are also seen. No presence of any atypical mitosis. Diagnosis of Nodular hidradenoma was given based on the cytological findings. For confirmation excision biopsy is done and tissue sent for histopathological analysis. A special stain like alcian blue (Figure 3) was also done. Histopathologic diagnosis of Nodular hidradenoma is given thereby confirming the cytological findings.

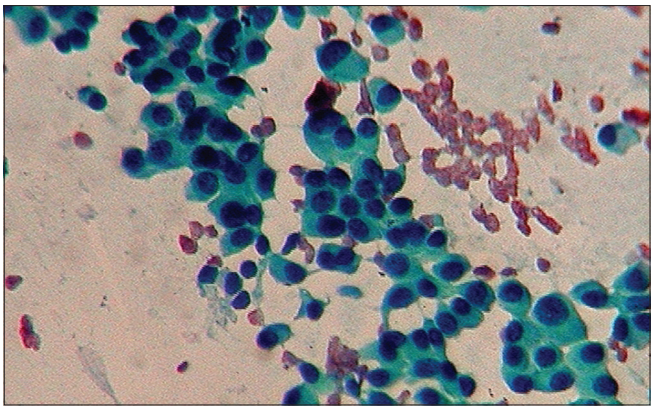

Figure 1: May-Grunwald-Giemsa stain shows variably sized overcrowded clusters of cells with variable amount of faintly stained cytoplasm, round to ovoid bland nucleus, inconspicuous nucleoli

DISCUSSION

Cytological diagnosis of nodular hidradenoma is rarely reported in the literature. Most cases of nodular hidradenoma are misdiagnosed, inconclusive, or misinterpreted on FNAC.

Smears are usually cellular containing a variably mixed population of two types of cells- eosinophilic/polygonal and clear cells. Eosinophilic cells contain round to ovoid nuclei, small nucleoli, with a moderate amount of faintly eosinophilic cytoplasm. Occasional cells show scanty cytoplasm with more basal cell-like appearance while some cells closely resemble squamoid cells. Clear cells have round eccentric nuclei, finely granular chromatin, small nucleoli and more abundant, water-clear cytoplasm. Mild hyperchromasia, aniso-nucleosides, and overlapping of nuclei with small prominent nucleoli were also seen. Eosinophilic cells formed large, cohesive, three-dimensional, papillary-like, closely packed clusters. Clear cells formed medium-sized, flat clusters. Rounded rosette-like formations and duct-like tubular structures were also seen. Extracellular hyaline material and amorphous material was present in the background. Histiocytes, fibroblasts, pigmented macrophages, foam cells, and naked nuclei may be seen.[6-13] The cytology of our case shows all the features reported previously except a prominent clear cell component. Scanty or absent clear cells may be the reasons for diagnostic pitfalls. The cytologic appearance of our case closely resembles that of adenoid cystic carcinoma, cutaneous cylindroma, and eccrine spiradenoma. Cytology of nodular hidradenocarcinoma shows cells with dense cytoplasm and basal cell-like appearance, cell sheets with squamous differentiation, necrotic debris, and multinucleated giant cells.[14]

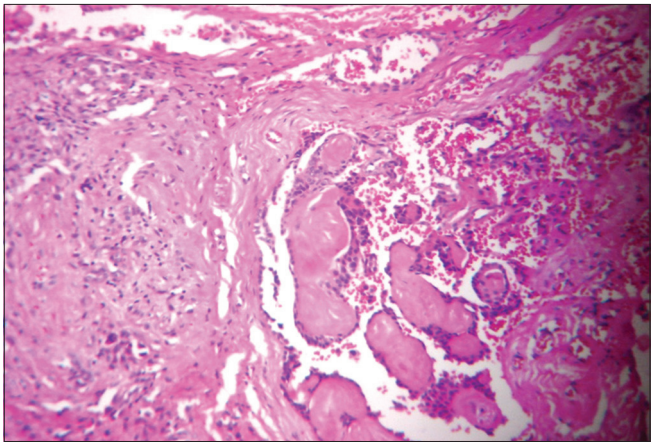

Figure 2: Hematoxylin and eosin stained section shows dark and light stained solid area with amorphous eosinophilic hyaline material filled cystic spaces lined by cuboidal cells

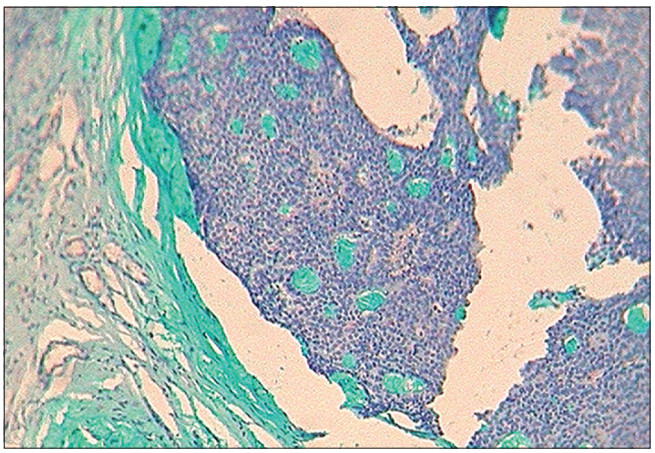

Figure 3: Alcian blue stain showing hyalinized stroma at places (×40)

Histologically, nodular hidradenoma is a well-circumscribed but unencapsulated solid cystic dermal tumor with a clear zone between the tumor and epidermis. Cystic spaces were filled with homogenous eosinophilic material. Solid areas comprised of eosinophilic and clear cells. Marked nuclear pleomorphism, hyperchromasia, and frequent or atypical mitoses are not observed.

Variants of nodular hidradenoma may show several types of cells. Clear cell hidradenoma, the most common variant consist predominantly of clear cells, with distinct cell borders. As the percentage of different cell types varies markedly in different tumors, cytopathologists should keep in mind the close resemblance of nodular hidradenoma to metastatic renal cell carcinoma, squamous cell carcinoma and hence these should be kept as a closest differential diagnosis.

CONCLUSION

To give a diagnosis of an adnexal tumor on cytology, adequate cellularity is of paramount importance. Cytologically the appearance of two types of cells, eosinophilic and clear cells in a papillary pattern along with ducts-like tubular structures and extracellular hyaline material in a cytology smear are the key features of nodular hidradenoma.

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Case Report

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Sturge–Weber Syndrome: A Case Report and Review of Literature

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Abstract

Sturge–Weber syndrome (SWS) is a rare congenital developmental, disorder manifesting with a facial port-wine birthmark, and a vascular malformation of the brain. It affects the skin in the distribution of the ophthalmic branch of the trigeminal nerve, abnormal capillary venous vessels in the leptomeninges of the brain and choroid, glaucoma, seizures, stroke, and intellectual disability. We reported a case of a 37-year-old male who had an unusual overgrowth of the left maxillary region, associated soft tissue hypertrophy directly corresponding to the distribution of the cutaneous port-wine stain, choroidal hemangioma, and hemianopsia of the left eye, hemiparesis of the right side of the body. Radiographic evaluation revealed tram-line like intracranial calcification, suggestive of SWS.

Key words: Choroidal hemangioma, Hemianopsia, Hemiparesis, Port-wine stains, Sturge–Weber syndrome, Tram-line like intracranial calcification

INTRODUCTION

Sturge–Weber syndrome (SWS) or encephalotrigeminal angiomatosis is a congenital, non-hereditary, condition of unknown etiology. The disease shows facial port-wine stain, ocular abnormalities (glaucoma and choroidal hemangioma), and leptomeningeal angioma.[1] It belongs to a group of the disorder known as the phakomatoses ("mother-spot" diseases). SWS was first described by Schirmer in 1860 and later more specifically by Sturge in 1879. He associated dermatological and ophthalmic changes of the disease to neurologic symptoms. Weber, in 1929, stated the radiologic alterations seen in patients of SWS.[2]

It is rare disorder occurring with no racial predilection[3] equally affecting males and females with 1:50,000 live births.[4] The classic features of SWS are angioma of the leptomeninges epilepsy, Port-wine stain, ocular involvement, dermal angiomas, mental retardation, hemiplegia, and abnormalities in skull radiographs.[5] Oral manifestations of the disease varies considerably. The morphological and histological changes in gingiva, pulp, and periodontium have been reported. However, the most common feature is a gingival hem-angiomatous lesion usually restricted to ipsilateral maxilla, mandible, lips, tongue, cheeks, palate, and floor of mouth.[1]

SWS are caused by the persistence of vascular plexus around the cephalic portion of the neural tube. The development of plexus starts during the sixth week of intra-uterine life and usually undergoes regression during the 9th week.[5] Angiomas of the leptomeninges are located in the parietal and occipital region and are usually unilateral. The presence of angioma alters the vascular dynamics causing precipitation of calcium deposits in the cerebral cortex. Seizures, mental retardation, hemiparesis, or hemiplegia develops secondary to this, and the severity depends on the extent of lesion.[6]

The cutaneous angiomas are called port-wine stains, which usually occur unilaterally along dermatomes supplied by the ophthalmic and maxillary division of trigeminal nerve. It may

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be bilateral or absent or may extend to the neck, limbs, and other parts of the body.[6] Involvement of the area supplied by ophthalmic division is pathognomonic of the disease. Ocular involvement results in glaucoma, choroidal hemangioma, buphthalmos, or hemianopsia (decreased vision).[7]

Intraorally angiomatosis may involve lips, gingival, buccal mucosa, palate, and floor of the mouth. The oral manifestations of SWS are port-wine stain lesion of oral mucosa and hyper vascular changes. Most common manifestation is the angiomatous lesion of gingiva that varies from slight vascular hyperplasia to massive hem-angiomatous proliferation. There is an increase in the vascular component and gingival hemorrhage at minimal trauma. The oral manifestations are unilateral and finish abruptly in the midline. Macroglossia and maxillary bone hypertrophy are seen in some patients leading to malocclusion and facial asymmetry. This syndrome is of rare occurrence and management becomes complicated due to risk of hemorrhage.[1]

In this report, we present a case of SWS with its characteristic manifestations.

CASE REPORT

A 37-year-old male patient reported to the Department of Oral Medicine & Radiology, Swargiya Dadasaheb Kalmegh Smruti Dental College and Hospital, Nagpur, Maharashtra, with a chief complaint of bleeding gums and pain in teeth and gums of upper and lower jaw. His past medical history revealed seizures, since 1 year of age, and lasted until the age of 15 years. He also gave the history of hemiparesis of the right side of the body at the age of 1 year and reddish discoloration on the left half of the face and neck since birth that became darker with the advancing age.

Patient's extra oral examination revealed facial asymmetry, overgrowth of the left maxillary regions, associated soft tissue hypertrophy directly corresponding to the distribution of the cutaneous port-wine stain involving V1 and V2 Distribution, and deviation of the nose toward the right side (Figure 1a and b). Pinkish red staining or so-called port-wine stains of left facial skin extending from the midline, involving forehead, nose, left half of upper lip and cheek (Figure 1a-c). The lower jaw, lower lip, and left ear were not involved. Similar type of stains seen on the left half of the neck, extending to left shoulder and left arm. Examination of the eye revealed hemianopsia and dilated blood vessels of the left eye. The right eye appeared to be healthy and patient was referred to the ophthalmologist for consultation. An angiomatous enlargement of the left upper lip was present.

Intraoral examination revealed erythematous, swollen attached gingiva involving the left maxillary arch soft in consistency, and restricted to the midline (Figure 2a and b). The Diascopy test was positive, suggestive of the angiomatous enlargement. Similar growth saw involving the left side of the palate extending to the midline (Figure 2c), areas of decapitation seen on the tongue (Figure 2d). Patient's oral hygiene was poor and showed chronic generalized periodontitis and generalized spacing resulting in malocclusion (Figure 2a and b).

Radiographic examination shows tram-line like calcification in the parietal lobe, on lateral skull projection (Figures 3 and 4) and posterior anterior skull radiograph (Figure 5). Based on the history, clinical findings and radiographic evaluation a diagnosis of SWS was made.

Figure 1: Port-wine stains in the distribution of trigeminal nerve

Figure 2: Intraoral photographs

Figure 3: Orthopantomogram

Figure 4: True lateral skull radiograph intracranial tram track calcification

Figure 5: Posterior anterior skull view osteohypertrophy of left maxillary bone

Blood investigations were found to be normal. Physician's consent taken before the extraction of Grade III mobile permanent mandibular right second molar and plaque control regimen started at regular intervals, proper instructions regarding maintaining oral health care, and use of chlorhexidine mouthwash were advised. Patient's evaluation after 1 month shows no evidence of gingival bleeding. Moreover, gingivectomy was planned for gingival enlargement. The patient is on follow-up. For the purpose of social acceptance, patients counseling was done to undergo treatment such as maxillectomy and laser treatment for facial stains.

DISCUSSION

SWS referred to as complete when both central nervous system and facial angiomas are present and incomplete when only one area is affected without the other. The Roach scale[8] for SWS is as follows:

Type I: Both facial and leptomeningeal angiomas; may have glaucoma
Type II: Facial angiomas alone; may have glaucoma
Type III: Isolated leptomeningeal angiomas; usually no glaucoma.

According to the Roach scale, our case is a Type I SWS. Leptomeningeal angiomas are unilateral lesions affecting the pia-arachnoid membrane over the posterior temporal, parietal, and occipital areas. It is typically a static lesion, but a review of literature also reveals some progressive lesions.[2] It commonly shows abnormal blood flow pattern as venous occlusion, thrombosis, vasomotor phenomenon, and vascular steal phenomenon resulting in cortical ischemia. This results in an epileptic convulsive crisis, transient hemiparesis, gliosis, and progressive deposition of calcium salts. These calcifications produce a characteristic double contoured "tram-line" appearance following the convolutions of the cerebral cortex. Brush field and Wyatt stated that these tram-line calcifications are pathognomonic of SWS.[9] These calcifications appear after the age of 2 years and remain stationary after the second decade of life. These calcifications are pyriform and curvilinear and most commonly seen in parietal and occipital lobes as seen in our case. These are best seen in the lateral skull view. If Magnetic resonance imaging (MRI) does not confirm the diagnosis in a suspected case of SWS, then computed tomography should be done because it is more likely to show calcification that can be elusive in MR imaging.[10]

Differential diagnosis includes Rendu-Osler-Weber syndrome, Maffucci's syndrome, angina-osteodystrophy syndrome, Von Hippel-Lindau disease, and Klippel Trenaumy-Weber syndrome.[6,7,10-12]

According to Inan and Marcus, the port-wine nevi are localized on the face, especially on the right side and are detected in 87-90% of the cases. The lesion extension over the middle line is seen in 50% of the patients, and bilateral involvement can be detected in about 33% of the cases.[13] In our case, the patient showed nevus flammeus only on the left side of the face without extension over the middle line.

CONCLUSION

The treatment of the Surge–Weber's syndrome is variable and depends on the presentation or intensity of its possible clinical features. The wide spectrum of clinical manifestations of SWS leads to multidisciplinary approaches for its management, such as Neurophysician, Ophthalmologist, Cosmetologist, Physiotherapist,

Radiologist, and Dentist. As a dentist, one must be aware of this condition and their possible complications arising during dental procedures and precautionary measures to avoid these complications.

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Case Report

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Primary Cervico-Vaginal B-cell Lymphoma with Immunohistochemical Confirmation: A Case Study

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Abstract

Non-Hodgkin's lymphoma (NHL) involving lower female genital tract is a rare event. Described presenting clinical symptoms in a literature in these patients are vaginal discharge and bleeding. Here with the report, a case of primary cervico-vaginal lymphoma in an old lady presenting with utero-vaginal (UV) prolapse. On clinical examination, there was second degree UV prolapse. Pelvic ultrasound showed a large hypo echoic mass involving the vagina with increased vascularity. To our surprise the sections from diffusely thickened vagina wall revealed high-grade round cell tumor which was diagnosed as NHL (B-cell type) by immunohistochemistry. To confirm primary vaginal involvement detailed clinical, radiological, and hematological examination was performed. The management of this disease is not well-defined in the literature. In our case, post-hysterectomy, no further treatment was offered to the patient; on 18 months follow-up she is doing well with no complaints.

Key words: Cervico-vaginal lymphoma, High-grade round cell tumor, Immunohistochemistry, Prolapse, Non-Hodgkin's lymphoma

INTRODUCTION

Primary extra nodal malignant lymphomas may occur in the female genital tract in about 30% of cases. Most of them are Non-Hodgkin's lymphoma (NHL) involving; in order of frequency are ovary (50%), uterus (30%), tubes (10%), vagina (6%), and vulva (4%).[1] Hence, NHL involving the vagina and moreover cervix as the primary site is extremely rare. The majority of NHLs arising at this site are high-grade lymphomas with diffuse large B-cell histotype.[2] Histomorphological differentials in these cases include poorly differentiated malignancies namely small cell variant of squamous cell carcinoma (SCC) and round cell tumors. Immunohistochemistry (IHC) is must to diagnose and confirm.

Though few cases have been reported in the literature all of these patients presented with vaginal discharge and bleeding.

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We came across such a diagnosis, but the presenting clinical symptom was utero-vaginal (UV) prolapse.

CASE REPORT

A 55-year-old postmenopausal lady, P_{3+1}, presented with complaints of something coming out of vagina from past 6 months, followed by persistent pain in the lower abdomen from past 4 months and post-menopausal bleeding since 20 days. There was associated burning micturition present. The patient was on medications for hypertension.

Her systemic examination was largely unremarkable. On per speculum examination, there was prolapsed uterus. Abdominal Ultrasound revealed cervix showing split anterior and posterior lips with a large hypo echoic mass filling the vagina showing vascularity with size of 5.4 cm × 3.7 cm × 6.0 cm. The lady was operated with a clinical diagnosis of UV prolapsed with suspicion of malignancy of cervix and/or vagina.

Total abdominal hysterectomy and bilateral salphingo-opeherectomy were done under general anesthesia. Intraoperatively, post-menopausal uterus measuring 5.7 cm × 4 cm × 2.6 cm, along with bilateral adnexa were

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found. The vagina was diffuse thickened. The specimen was sent for histopathological examination.

We received hysterectomy with bilateral salphingo-opeherectomy. Uterus measured 8.5 cm × 4 cm × 1.5 cm with posterior wall thickness measuring 1 cms, on gross. Cervical lips were grossly hypertrophied and elongated. The vagina was thickened and rubbery; measured 3 cm in length with a wall thickness of 1.8 cm (Figure 1a). Both the ovaries and fallopian tubes were unremarkable on gross.

Representative tissue pieces were embedded, processed, stained with hematoxylin and eosin and examined microscopically. Sections from the cervix and vagina showed flattened lining along with infiltration of cervical and vaginal stroma by medium to large abnormal round to oval tumor cells with the high nucleo-cytoplasmic ratio, clumped chromatin, prominent to inconspicuous nucleoli, and scant amount of cytoplasm, intermixed with few reactive mature lymphocytes (Figure 1b and c). Surgical resection margin of the specimen was free from tumor infiltration. The section from the uterus showed endometrium in the secretory phase. Sections from the bilateral adnexa showed normal histology.

Morphological differentials which were considered were a high-grade epithelial tumor, small cell variant of SCC, NHL, high-grade mesenchymal tumor, adnexal tumor, malignant melanoma, high-grade neuroendocrine tumor. Tumor cells were negative for cytokeratin (Figure 2c), desmin, S-100, HMB-45, chromogranin, and CD99. There was diffuse immunoexpression for leukocyte common antigen (Figure 1d) with focal vimentin expression. For definitive typing after immunohistochemical confirmation of Lymphoma added IHC CD3, CD20, CD5, and CD10 was done. Diffuse immunoexpression of CD20 (Figure 2a) was seen with background cells displaying CD3 (Figure 2b) expression. All other markers were negative (Figure 2c and 2d).

CT whole abdomen, positron emission tomography (PET) scan with bone marrow aspiration and biopsy were performed. No uptake was found on PET scan. There was no lymphadenopathy (abdominal or retroperitoneal) on CT. Bone marrow smears showed normoblastic hematopoesis.

Finally, diagnosis of primary cervico-vaginal B-cell lymphoma was made. As the disease was limited to cervix and vagina only and there was further uptake on PET, the patient was kept under conservative management. On 18 months follow-up, the lady is completely asymptomatic.

DISCUSSION

Primitive lymphomas are unexpected diseases in the female genital tract, particularly in the uterus and vagina; therefore,

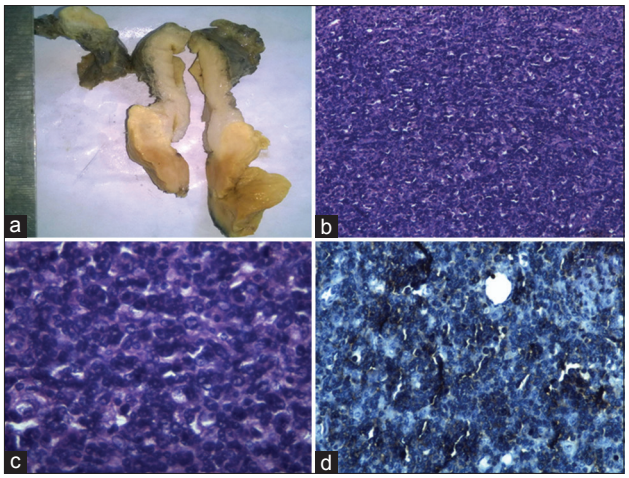

Figure 1: Gross specimen showing atrophic uterus, along with hypertrophied and elongated cervical lips and vaginal wall with a waxy appearance (a). H and E section shows the diffuse arrangement of monomorphic round cells with no intervening stroma ×40 (b), with higher magnification view in (c), ×400. Tumor cells show immunoexpression for leukocyte common antigen in (d) ×100

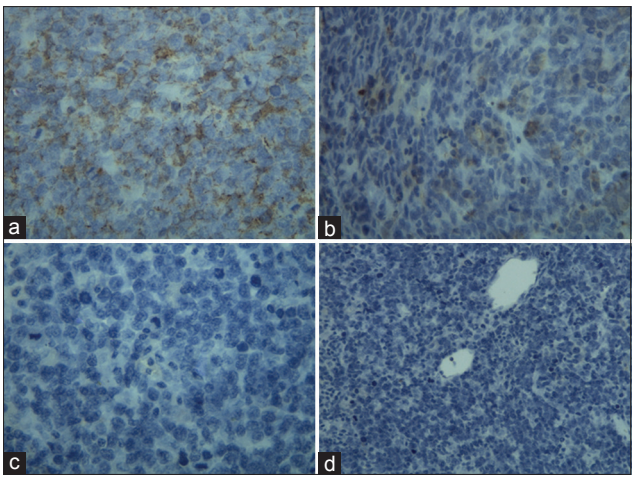

Figure 2: Abnormal lymphoid cells showed diffuse immunoexpression for CD20 (a), there were few scattered cells in background which were positive for CD3 (b). But, there was no immunoexpression for cytokeratin and CD10 (c and d)

they are likely to be misdiagnosed as either inflammatory diseases or other types of malignancies.[3] NHL should be suspected there is diffuse infiltration by monomorphic cell population with clumped chromatin and conspicuous to inconspicuous nucleoli and scant cytoplasm complimented with thickened homogenous waxy thickening on gross (Figure 1a-c). But, then also definitive confirmation by IHC should be performed in all suspected cases.

The age at presentation ranges from 20 to 80 years, with the median age varying from 40 to 59 years. 70% of these tumors are of diffuse large cell type, and 20% are low-grade follicular lymphomas.[4] The present lady was the 55-year-old female. Most frequent clinical symptom associated with

vaginal lymphomas reported is discharge or bleeding per-vaginum. Our case is unusual that the mass caused UV prolapse instead. The present case was diffuse large B-cell lymphoma, morphologically the tumor cells were medium to large, and there was frequent mitotic activity. The tumor was limited to vagina and cervix; the best part was that unknowingly complete excision of the tumor was made on the initial surgery.

The histology of cervico-vaginal lymphomas is similar to that observed in the primary nodal presentation. The prognosis of uterine and vaginal lymphomas is relatively good, particularly when compared to ovarian lymphoma: Overall survival is over 70%, which is fully comparable with other extra nodal presentations and far better than that of ovarian localization (30%).[3]

It is due to the lack of agreement regarding the effectiveness of various modalities as a consequence of its low incidence. Treatment of lymphoma of the cervix may involve irradiation therapy alone, irradiation combined with hysterectomy.[2] Few authors have reported the successful management of by neo-adjuvant chemotherapy alone.[5] But as no post-surgery uptake was seen on PET scan, the patient was kept on conservative management. Post complete removal of the tumor mass the patient is apparently asymptomatic on 18 months follow-up evaluation.

CONCLUSION

Our case was unusual clinically as even on ultrasound the patient was not suspected to have NHL; moreover, there was no lymphadenopathy. Only histopathology and IHC could diagnose; moreover, we support the present literature that cervico-vaginal involvement by NHL is a rare event, but the over-all prognosis of the patient is good if the disease is limited.

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Case Report

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Adrenal Insufficiency Mimicking Gastrointestinal Disorder: A Case Report

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Abstract

Adrenal insufficiency is a rare disease with varied and non-specific clinical manifestations. Tuberculosis is one of the major causes of adrenal insufficiency in many developing countries. Effect of tuberculosis may be evident even after several years of affection of the gland. Acute tuberculosis of the adrenal gland may result in enlargement of the gland, but chronic tuberculosis may shrink and calcify the gland. The diagnosis may be delayed if the clinical presentation mimics a gastrointestinal disorder or personality changes resembling a psychiatric illness. The disease carries a high degree of morbidity and mortality if not recognized and treated in time.

Key words: Adrenal insufficiency, Crisis, Gastrointestinal, Shock, Tuberculosis

INTRODUCTION

Adrenal insufficiency (Addison's disease) is a rare disease with an incidence of 0.8/100,000 cases.[1] The clinical presentation of the disease is varied and non-specific[2] and hence a diagnostic and therapeutic challenge for the consulting physician. The tuberculous affection of the adrenal gland is one important cause of adrenal insufficiency, especially in the developing countries. Tuberculosis may involve many endocrine glands including the hypothalamus, pituitary, and thyroid.

Adrenal gland may be involved by hematogenous spread of infection or rarely by primary involvement of adrenal gland.[3] The rich blood supply and suppressed immune response locally due to high concentration of corticosteroids make adrenal gland an easy target for Mycobacteria.[4] Post-tuberculous adrenal insufficiency may be diagnosed in acute, chronic phase, or during an episode of adrenal crisis. Sub clinical adrenal insufficiency observed during active pulmonary tuberculosis can reverse with treatment.[5] Addison's disease presents with gastrointestinal (GI) complaints in 20% of cases. The GI symptoms of adrenal insufficiency may be anorexia, nausea, vomiting, weight loss, constipation, diarrhea, and abdominal pain, especially during adrenal crisis mimicking an acute abdomen.

In addition to estimation of the adrenal reserve by cortisol estimation, imaging modalities such as computed tomography (CT) scan and magnetic resonance imaging of adrenals may aid in the assessment of the gland structure. A high index of clinical suspicion is a mainstay for the diagnosis of the disease and failure to recognize early carries a high rate of mortality if not treated in time. We report a case of a young boy who presented to us in a state of shock with preceding GI symptoms.

CASE REPORT

A young man aged 24 years was admitted with a history of fever, altered sensorium, abdominal pain, and vomiting of 2 days duration. The patient was having vomiting and episodes of diarrhea on and off, dyspepsia, and failure to gain weight for the past 6 months for which he had undergone various investigations including upper GI endoscopy, which was normal. He was treated on various

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occasions symptomatically with no lasting improvement. He was treated for pulmonary tuberculosis 1½ years back and was declared cured.

At the time of admission, the patient was febrile (101°F), conscious but drowsy, minimally responding to commands. There was no neck stiffness. He appeared dehydrated. His supine blood pressure was 60/30 mmHg, pulse 100/min regular. The boy was of dark complexion with hyperpigmentation evident over both palms (Figure 1a), tongue (Figure 1b) and a hyper pigmented scar (Figure 2). The fundoscopic examination was normal.

Investigations revealed the following findings: Hemoglobin - 14.3 g/dl, total leucocyte count-16500 cells/cu.mm, differential count-polymorphs - 68, leucocytes – 30, and eosinophils - 2% platelet count - 2, 52, 000 cells/cu.mm.

Random blood glucose - 62mg/dl, blood urea - 56 mg/dl, serum creatinine - 2 mg/dl, serum sodium - 122 meq/L, serum potassium - 5.5 meq/L, serum chloride - 89 meq/dl, and HCO_3 - 22 meq/dl.

Liver Function Tests

Total bilirubin - 0.7 mg/dl, direct bilirubin - 0.2 mg/dl, serum glutamic oxaloacetic transaminase - 43 IU/L, serum glutamic-pyruvic transaminase - 28 IU/L, alkaline phosphatase - 89 IU/L, total protein - 6.1 g/dl, albumin - 3.4 g/dl, HIV 1, and 2 (enzyme-linked immunosorbent assay) negative. Blood and urine culture - sterile, electrocardiography - sinus tachycardia.

X-ray chest posterior-anterior view-normal, CT brain (plain) normal study, ultrasonography abdomen-normal.

Random serum cortisol (chemiluminiscence immuno assay) - 0.19 mcg/dl (6.2-19.4 mcg/dl).

CT Abdomen

Bilateral atrophic and calcified adrenals due to tuberculous granulomatous lesions (Figure 3).

This patient was managed with normal saline dextrose infusion, inotropes, and antibiotics initially. The patient continued to be in hypotension for 4 h. In view of past history of tuberculosis with hyper pigmented lesions, adrenal insufficiency was suspected and after collecting serum sample for cortisol, the patient was started on hydrocortisone 100 mg IV Q6H following which the patient improved dramatically.

A final diagnosis of Addison's disease due to the post-tuberculous destruction of adrenal gland was made. The patient was discharged with oral prednisolone

Figure 1: (a) Hyperpigmentation of palms, (b) shows hyperpigmentation of tongue

Figure 2: Hyperpigmented scar

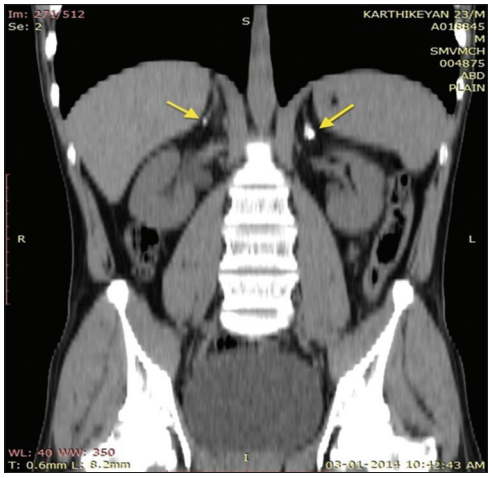

Figure 3: Bilateral adrenal calcification (left > right)

40 mg/day and reduced to 10 mg/day over 4 weeks with mineralocorticoid supplementation, fludrocortisone 0.05 mg/day. He was also educated about stress dose of steroids. He is doing well and is on regular follow-up.

DISCUSSION

Adrenal insufficiency (Addison's disease) is a rare disease with varied, non-specific manifestations.[2,3] The common manifestations are fatigue, anorexia, weight loss, vomiting, skin hyperpigmentation (80%), diarrhea (20%), craving for salt, personality changes, and fulminant shock. 90% of the adrenal gland must be destroyed before insufficiency develops.[6] If not recognized early and treated in time can lead to considerable mortality.[7]

Adrenal gland maybe involved in tuberculous, fungal, viral, or parasitic infections. Though autoimmune involvement of the adrenal gland is common in developed countries,[8] tuberculosis still remains an important cause of adrenal insufficiency in India and other developing countries.[9] The presence of vitiligo may point towards an autoimmune etiology of adrenal insufficiency.

The adrenal gland affected commonly by hematogenous spread of tuberculous infection may initially enlarge and finally get fibrosed and shrink in size and become calcified.[10-12]

The adrenal gland affected by tuberculosis may recover its function following treatment with anti tuberculous drugs, but adrenal insufficiency maybe evident even years after treatment.[13,14] Adrenal crisis is precipitated by infection, dehydration, withdrawal of steroids, surgery, or trauma. Adrenal crisis is the cause of death in 5% of the patients.

Our patient who was treated for pulmonary tuberculosis earlier presented with adrenalcrisis 1½ years following completion of treatment. Since the disease presents with various non-specific symptoms, the diagnosis was delayed until the patient presented with adrenal crisis.[15] Our patient had GI symptoms predominantly and was getting empirical treatment with no permanent relief. Studies have shown that patients with predominant GI symptoms presented most often with the crisis.[16] Diagnosis may be delayed for a variable period ranging from 6 months to more than 5 years when the patient may present with adrenal insufficiency or crisis.[17] Past history of tuberculosis, hyperpigmentation of the palms, palate and the resistant shock, and electrolyte abnormalities guided us toward the correct diagnosis. It is ideal to dorapid adrenocorticotropin stimulation test to confirm the diagnosis. A serum cortisol level of >20 μg in 60 min following administration of 250 μg of cosyntropin rules out primary adrenal insufficiency. In emergency situations, if random cortisol is <3 mcg/dl, hypo function of the adrenals is confirmed[17] as was the case in our patient.

CONCLUSION

Adrenal insufficiency should be suspected and investigated in any patient with unexplained weight loss and GI symptoms since failure to diagnose the disease in time may lead to considerable morbidity and mortality. Primary care physicians should be aware of this disorder, and a thorough general examination would help in early detection of the cases and institution of appropriate treatment.

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