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Detection of Left Atrial Enlargement by Echocardiography and Electrocardiogram Correlation in Cardiac and Non-cardiac Diseases

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INTRODUCTION

Left atrial enlargement (LAE) is a marker for severity and chronicity of diastolic dysfunction:

During ventricular diastole, LA is directly exposed to left ventricular (LV) pressures through the open mitral valve. With worsening LV compliance, LA pressure increases to maintain adequate LV filling, which results in LAE. LA volume overload resulting from mitral valve regurgitation, arteriovenous fistula, left to right shunt, or high cardiac output state can also contribute to LA chamber remodeling. Therefore, LA volume may reflect the severity of diastolic dysfunction. LA remodeling may also represent the chronicity of exposure to abnormal LV filling pressure. Thus, LA volume as a reflection of severity and chronicity of diastolic dysfunction provides prognostic information incremental to that of diastolic function class determined by multiple load dependent Doppler parameters reflective of instantaneous LV diastolic function and filling pressures.

Original Article

Abstract

Introduction: Left atrial enlargement (LAE) is an important pathologic change in many forms of heart disease. There is growing recognition of an association between LAE and increased morbidity and mortality in patients with cardiovascular diseases.

Materials and Methods: This study was undertaken from July 2014 to August 2015 in all medical units of Mahatma Gandhi Memorial Hospital, Warangal, 120 randomly selected cases of suspected LAE were studied using two-dimensional echocardiography (ECHO), and it was compared with an electrocardiogram (ECG).

Results: In the present study, age of the patient ranges from 17 to 90 years with mean age of 49.21 years. Most of the cases have rheumatic mitral and aortic valve disease (45%) followed by hypertension (18.3%) and ischemic heart disease (13.3%). Criteria “Duration of negative phase of P-wave in lead V₁” have the highest sensitivity 87.5%. Criteria of LAE “P-wave notching” have the highest specificity 100% for detection of LAE in ECG.

Conclusion: Morris index P-terminal force in precordial lead V₁ is the best criterion having sensitivity 85% and specificity 95%. The sensitivity of various ECG criteria of LAE shows variable response, but specificity remains constant at progressively higher ranges of LA dimension.

Key words: Echocardiogram, Electrocardiogram, Left arterial enlargement
Therefore, LA volume has been termed “glycosylated hemoglobin of diastolic dysfunction.”

Several large population-based prospective studies have shown a strong association between M-mode anteroposterior LA diameter and the risk of new onset AF.\(^5^,^6\)

In the Framingham Heart Study, every 5 mm increase in LA diameter increased the development of AF by 39%, while the cardiovascular (CV) health study showed a four-fold increase in the risk of new AF with LA diameter 0.5 mm.\(^5\)

Evidence from these studies indicates that LA size encompasses information not captured by clinical data or one-dimensional M-mode assessment and thus represents a superior predictor of outcomes including AF.\(^7^,^8\)

In recent trials such as the Losartan Intervention for Endpoint reduction in hypertension trial, LA diameter/height predicted the risk of CV events independent of other clinical risk factors in hypertensive patients with LV hypertrophy.\(^1^0\)

Similarly, in a very large study of patients referred for echocardiography (ECHO), LA volume index predicted all-cause mortality independent of LV geometric patterns. The prognostic implication of LA size has also been shown in high-risk subgroups, such as patients with acute myocardial infarction, atrial arrhythmia, LV dysfunction, or dilated cardiomyopathy, and patients undergoing valve replacement for aortic stenosis and mitral regurgitations.\(^1^1\)

So, the size of the LA is an important index of cardiac status.

Electrocardiography (ECG) is a simple, non-invasive, cost-effective, accessible, and reproducible means to diagnose increased LA size as well as serial follow-up evaluation.\(^2\)

X-ray studies measure only gross changes in atria.\(^1^2\)

Angiography is a better method of demonstration of LA contour and permits more accurate measurements. However, it has limited utility in evaluating large populations due to its invasive nature and complex procedure.\(^1^3^,^1^4\)

ECHO is comparable to angiography in assessing LA size.\(^1^5\) Being an accurate and non-invasive technique for obtaining anatomical measurements, it is the universally accepted.

### Diagnostic Standard

LA volume has been measured using three-dimensional ECHO and has shown good correlation with other methods including magnetic resonance imaging.

However, in the Indian setting, ECG is widely used and has added advantage over ECHO in being cost-effective, easily available, and accessible.

### MATERIALS AND METHODS

#### Study Setting and Duration

This study was undertaken from July 2014 to August 2015 in all medical units of Mahatma Gandhi Memorial Hospital, Warangal. This was a prospective cross-sectional study. The study group comprised 120 randomly selected patients who are referred for two-dimensional (2D) echo.

Patients with age <14 years, pericardial effusion, chronic obstructive pulmonary diseases, usage of drugs such as beta blockers, digitalis, calcium channel blockers, AF, and conduction defects.

120 suspected cases of LAE were subjected to the following: Detailed history taking, general physical examination, systemic examination, ECG, and 2D ECHO.

The number of true positives, true negatives, false positives, and false negatives was calculated for the individual ECG criteria as parameters of diagnostic accuracy, sensitivity, specificity, positive predictive value, and negative predictive value were calculated. Studies of correlation were done for absolute value of LA (obtained by echo) with P-wave duration in lead II, duration of the negative phase of P-wave in lead V\(_1\), and depth of negative phase of P-wave in lead V\(_1\). In each case, the Pearson's correlation coefficient was calculated.

### RESULTS

Age of the patient ranges from 17 to 90 years with mean age of 49.21 years. There were 72 females and 48 males.

In this study, most of the cases have rheumatic mitral and aortic valve disease followed by hypertension, ischemic heart disease (IHD), isolated aortic valve disease, cardiomyopathies, mitral valve prolapse, and thyrotoxicosis (Tables 1-3).

- Sensitivity: 87.5%
- Specificity: 85%
- Positive predictive value: 92.1%
- Negative predictive value: 77.2%
- Pearson correlation coefficient: 0.51.
DISCUSSION

Size of the LA is an important index of cardiac status. LAE has important implications such as the development of AF, thromboembolic phenomena, and complications thereof.

The LA is affected directly by increased ventricular filling pressure, increased resistance across the mitral valve, or volume overload caused by mitral valve regurgitation. ECG could offer a simple, cost-effective, readily available, non-invasive means to diagnose LAE if reliable criteria were available.

The criteria used in the present study are the ones most frequently used clinically and received attention in the existing literature either individually or in groups.

However, certain ECG abnormalities traditionally attributed to LAE may occur in patients with LA pressure overload or defective atrial conduction or both.

Previously, it had been established that LA thickening with or without dilatation could produce some of the ECG signs examined in this study. These findings suggest that the diagnostic accuracy of previously described ECG criteria for LAE may be more limited than was previously appreciated.

Our study group comprised 120 suspected cases of LAE in normal sinus rhythm; 54 of them suffering from rheumatic heart disease; 40 were females and 14 were males. This finding well correlates with the previously documented higher incidence of rheumatic heart disease in female population.

This also explains the larger number of females among the 120 consecutive patients suspected having LAE since the majority of them were suffering from rheumatic heart disease.

P-wave duration in lead II >110 ms has the sensitivity of 62.5%, specificity 80%, positive predictive value 86.2%, and negative predictive value 51%.

In the present study, correlation of P-wave duration in lead II with LA dimension obtained by ECHO has yielded a moderately positive correlation with a correlation coefficient of 0.2. In most others studies, correlation with LA size has been positive with correlation coefficients of 0.56-0.74.

Our lower degree of correlation may be due to the exclusion of patients with AF, who usually have LA size >45 mm.

In our study, age of the patients ranged from 17 to 90 years with mean age of 49.21 years. There were 60% females and 40 males with a ratio of 1:1.5 showing female preponderance. Waggoner et al. in their study involving 339 patients; 58.99% were females and 41.01% were males.

Hazen et al. study ECGs and surface ECHO obtained within 1 week of each other were evaluated in 551 patients (140 normal and 411 study subjects). The various P-wave morphologies were found to be poorly sensitive (30-60%) but very specific (90%) for LAE. Combinations of P-wave morphologies did not improve sensitivity or specificity. ECG features did give an estimate of the degree of LAE. When P-terminal force in precordial lead V1 (PTFV1) is ≥ imsec mm, 95% of patients had LA size ≥40 mm; and when this parameter was ≥4 mimsec mm, 75% had LA size ≥60 mm. These criteria for LAE on the ECG are specific and predictive of the degree of LAE measured by ECHO.

In Mishra et al. (2008) study, ECGs and ECHO were obtained in 100 consecutive patients suspected of having LAE due to different underlying heart diseases.
The diagnostic accuracy of six ECG criteria of LAE was evaluated comparing with LA size in M-mode ECHO study. Various criteria were found to be poor to mildly sensitive (8-78%) but highly specific (85-100%) for LAE.

Morris index (PTFV) was found to be the best criterion having 76% sensitivity and 92% specificity. Combination of criteria enhances the sensitivity at the cost of specificity. Overall predictive index of ECG for LAE is not encouraging.

A study by Chirife et al. showed that ECG positivity of 89% when P-wave duration was considered alone, ECG positivity of 83% when Morris index was considered alone, and ECG positivity of 89% when Macruz index alone was considered.

Waggoner et al. showed that overall ECG predictability of LAE was 80% and showed 100% positivity when LA size was >50 mm, 70.83% positivity when LA size was 46-50 mm, and 56.41% positivity when LA size was 41-45 mm. Hence, our study is comparable to these studies.

PTFV >40 mm yielded sensitivity 85%, specificity 90%, positive predictive value 94.4%, and negative predictive value 75%. Its value in detection of LAE has been reasonably well established with sensitivity reported as 67-89% and specificity 83-94% which is in general agreeable to our findings.

On the other hand, Romhilt et al. did not find PTFV to be a sensitive criterion (only 44%). However, the reason for this low value is unclear. Aronow et al. found the sensitivity to be 32% and specificity 94%. This low sensitivity is probability related to a higher mean age of their study population, i.e., 82 ± 8 years.

Jose et al. have calculated its positive predictive value as 85% which is nearby the value obtained by our study.

In the present study, we have minimized error by excluding sources of error like patients with AF and conduction defects. Furthermore, errors of measurement have been minimized by taking some complexes at higher paper speed, i.e., 50 mm/s and measuring through five power magnifying lens.

The predictive value indicates the diagnostic power of a test.

In our study, the various ECG criteria of LAE have positive predictive value of 90%-100% and negative predictive value of 28-58%. These indices of diagnostic accuracy have not been specifically mentioned in the available literature.

The correlation coefficients (r) obtained were 0.2 for P-wave duration >0.11 s, 0.51 for criteria duration of the negative phase of P-wave in lead V1, and 0.17 for criteria depth of negative phase of P-wave in lead V1.

The duration of the negative phase of P-wave in lead V1 correlates best with LA size obtained by ECHO.

Abnormalities in atrial conduction resulting from hypertension, elevated pulmonary capillary wedge pressure, or intrinsic conduction defects are associated with abnormalities in the P-wave and may be independent of atrial size. However, previous studies have shown that many patients with LAE also have LA pressure overload or defective atrial conduction. Thus, in many patients, it may be difficult to sort out the exact origin of the ECG criteria traditionally attributed to LAE. Lee et al. have even suggested using the term “non-specific LA abnormalities.”

LAE is a frequent accompaniment of rheumatic mitral valve disease, where LA pressure is also increased.

So, the mere presence of an enlarged LA or elevated LA pressure does not establish the primacy of either in the genesis of this electrocardiographic pattern. The role of atrial inflammation or scaring or both (as part of the disease process) can also produce ECG abnormalities of LAE by causing conduction defects. In our set up, the majority of patients suspected of having LAE had rheumatic mitral valve disease.

In patients with IHD, the ECG pattern of LAE produced may also be due to increased LV end diastolic pressure or may be due to ischemia or infarction or both.

CONCLUSION

The use M-mode ECHO as a diagnostic standard represents a minor limitation because extreme angulation of the transducer may produce alteration in LA diameter.

We sought to minimize such artifactual measurement by performing ECHO only from windows in the third or fourth intercostal spaces (left sternal border) and by measuring LA size only at the level of the aortic valve leaflets.

REFERENCES


Can Microalbuminurina Predict the Outcome (Mortality) in Critically ill Patients? A Hospital-based, Prospective, Observational Study

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Abstract

Background: Complex scores, such as Acute Physiology and Chronic Health Evaluation II (APACHE II) scores, are highly reliable methods of to predict the mortality in critically ill patients. However, due to their complex nature intense resource requirements, their utility is limited in resource-poor settings like India. Hence, low-cost reliable markers like microalbuminurina can be utilized in such situations. Hence, the present study intends to assess the role of microalbuminurina in predicting the mortality among critically ill patients.

Materials and Methods: The study was a prospective observational study, conducted in a medical-surgical intensive care unit (ICU) of a private tertiary care teaching hospital. A total of 50 adult patients (>18 years) with a stay in the ICU for more than 24 h were included. For disease severity scoring, urinary microalbumin will be measured using the immunoturbidimetric method with an albumin creatinine ratio cutoff of 30-300 mg/L.

Results: The mean microalbumin level was 25.39 g/dl higher in people who met with mortality, compared to people who survived (95% confidence interval [CI]: 43.57-94.37, \(P < 0.463\)), which was statistically not significant. The mean microalbumin level was 25.39 g/dl higher in people who met with mortality, compared to people who survived (95% CI: 43.57-94.37, \(P = 0.463\)), which was statistically not significant. The area under receiver operating characteristic curve for microalbumin in predicting mortality was 0.59 (95% CI: 0.41-0.772, \(P = 0.398\)) and was very close to the null value of 0.5% and 95% CI included the null value of 0.5.

Conclusions: To conclude, the findings reveal that microalbuminurina weakly correlated with the mortality of the ICU patients and that the APACHE II scores may be more reliable and accurate measure, though it employs cumbersome data collection methods and complex statistical analysis.

Key words: Micro albumin, Critically ill, Mortality, Prediction

INTRODUCTION

The systemic inflammatory response is usually widespread and severe in patients with critical illnesses, sometimes in advanced cases may result in multiple organ failures and eventually death.¹ Systemic inflammatory response syndrome (SIRS), as the name suggests, is a consequence to a variety of acute pathological conditions such as hemorrhagic shock, sepsis, multiple trauma, or pancreatitis.² Precise prediction of the outcome of critically ill patients and the best use of the intensive care unit (ICU) resources have been the objectives of studies since many years.³ Such measures enable the intensivist to prepare for accurate and aggressive therapeutic interventions by early identification of patients most at risk of life-threatening outcomes and also suitable counseling of the family members and/or the patient.

Numerous markers or methods have been utilized as prognostication tools for managing such patients thereby effectively the mortality both short- and long-term. Acute Physiology and Chronic Health Evaluation (APACHE) II and Simplified Acute Physiology Score (SAP) II scores are two of the most commonly used methods to predict the
mortality but have found to be of limited value for daily practical purposes due to their complex nature, though they have been efficient in evaluating the outcome.\textsuperscript{1,3,4}

The measures used in ICU should ideally be sensitive, inexpensive, preferably detect short-term changes that can produce rapid and reliable results including the impact of therapeutic outcomes on the patients.

Considerable research has shown that various reliable short-term markers have been assessed among such patients, though to a variable degree. Red cell distribution width is one such measure, which has been found to be an inexpensive, robust predictor of patient mortality.\textsuperscript{5} Similarly, elevated levels of blood urea nitrogen,\textsuperscript{6} blood glucose amplitude variability,\textsuperscript{7} extravascular lung water index,\textsuperscript{8} CD8(+) T-cell counts,\textsuperscript{9} sequential organ failure assessment (SOFA),\textsuperscript{10} and microalbuminuria levels\textsuperscript{11} are some of the commonly used markers having varying degree of applicability.

Microalbuminuria is a common consequence to numerous inflammatory conditions such as burns, meningitis, pancreatitis, myocardial infarction, and cerebral ischemia. Several studies have consistently shown that microalbuminuria is a simple, suitable, non-invasive, and inexpensive predictor of mortality, which can be used as a bedside tool in critically ill patients.\textsuperscript{11-14} In fact, its utility and efficiency are found to be equal to APACHE II score, a standard but complex tool in predicting the ICU patient mortality.\textsuperscript{12} In countries like India, where the sophisticated and cost demanding therapeutic interventions are scarce, effective determination, and monitoring of optimal treatment procedures and patient mortality is of utmost importance. Hence, low-cost reliable markers like microalbuminuria can be utilized in such situations; hence, the present study intends to assess the role of microalbuminuria in predicting the mortality among critically ill patients.

**Objectives**

The goal of our study is to evaluate whether microalbuminuria (albumin creatinine ratio [ACR]). Measured within 6 h of ICU admission is as effective as the APACHE II score to predict outcome in critically ill patients.

**MATERIALS AND METHODS**

- **Study design:** The study was a prospective observational study
- **Study setting:** The study was conducted in a medical-surgical ICU of a private tertiary care teaching hospital
- **Study population:** The study was conducted on adult patients admitted to ICU

- **Sample size:** A total of 50 study participants were included in the study
- **Sampling method:** All the eligible subjects were included sequentially into the study, hence no sampling was done.

**Inclusion and Exclusion Criteria**

All adult patients (>18 years) with a stay in the ICU for more than 24 h were considered for inclusion into the study. Exclusion criteria - Patients with anuria, macroscopic hematuria, preexisting chronic kidney disease, female patients with menstruation, pregnancy. Retrospectively, patients with marked proteinuria due to renal and post-renal causes, for example, urinary tract infection and previously undiagnosed chronic renal failure will be excluded.

**Study Procedure**

On admission, demographic data were collected for each patient such as age, gender, date and time of admission, patient’s clinical classification (medical or surgical), provisional diagnosis, co-morbid conditions such as diabetes, hypertension, and chronic kidney disease. For disease severity scoring, APACHE II score was calculated from data collected during the first 24 h following ICU admission. ABG analysis is done using i-STAT system (Sandor Medicals Pvt., Ltd.) Each patient will be followed up throughout their ICU stay and the following outcome data obtained; ICU length of stay and mortality. At the time of admission, patients were examined for vital signs and symptoms of SIRS, organ failure, and/or infection. Culture samples sent and antibiotics received within 24 h of admission to be noted. Infection is defined by the presence of clinical signs of SIRS along with an identified source of infection and/or positive blood cultures. The American College of Chest Physicians/Society of Critical Care Medicine Consensus Conference definitions is used to identify patients with SIRS, sepsis (SIRS with infection), septic shock (sepsis with hypotension on vasopressor support), and multiorgan dysfunction syndrome. Glomerular filtration rate is estimated using Cockcroft-Gault formula. Spot urine samples were collected within 6 h of admission for quantification of ACR. The ACR test had already been in general use in the lab before the study started. Urinary microalbumin will be measured using the immunoturbidimetric method (Turbilyte Ma-Tulip Diagnostics (P) Ltd. Goa, India). Microalbuminuria is defined as ACR of 30-300 mg/L. The ratio has a conventional cutoff value of 20 mg/L in the healthy reference population. The reference range for mortality prediction in critically ill population is yet to be determined. Statistical analysis of results will be done to assess the sensitivity and specificity of the study. The
clinical outcomes were compared with the APACHE II Scores and microalbuminuria levels statistically.

**Ethical Considerations**

The study was approved by Institutional Human Ethics Committee. Informed written consent was obtained from the legal guardian of the study participants after explaining the purpose of the study, risks, and benefits involved. The personal data of the participants were kept confidential throughout the study period.

**Statistical Analysis**

Mortality was the primary outcome variable in the study. Urine albumin levels and APACHE II score were considered as primary explanatory variables. Various sociodemographic, clinical, and laboratory parameters were considered as other explanatory variables. Descriptive analysis of the explanatory and outcome variables was done using mean and standard deviation for quantitative variables, frequency, and percentages for categorical variables. The correlation between microalbumin levels and APACHE II score was assessed by Spearman rank correlation and its P value. Receiver operating characteristic (ROC) analysis was done to assess the validity of microalbumin predicting mortality. The sensitivity, specificity, and predictive values for various cutoff levels of microalbumin were calculated. IBM SPSS version 21 was used for statistical analysis.

**RESULTS**

A total of 50 participants were included in the final analysis.

The mean age of study participants was 53.14 years. Males and females constituted 52% and 48% of the study participants, respectively. The incidence of mortality in the study population was 18% (Table 1 and Figure 1).

The mean microalbumin level was 25.39 g/dl higher in people who met with mortality, compared to people who survived (95% confidence interval [CI]: 43.57-94.37, P < 0.463), which was statistically not significant. The mean APACHE II score was 14.56 in people with mortality, compared to 10.80 in people who survived (mean difference - 3.75, 95% CI: 0.15-7.34, P = 0.041), which was statistically significant (Table 2).

There was very weak positive correlation between urine microalbumin and APACHE-II score in the study population (correlation coefficient r = 0.199, P = 0.166).

The area under ROC curve for microalbumin in predicting mortality was 0.59 (95% CI: 0.41-0.772, P = 0.398) and was very close to null value of 0.5 and 95% CI included the null value of 0.5 (Figure 2).

**DISCUSSION**

The inflammatory reaction initiated in response to SIRS is usually severe and sustained that can induce rapid and profound changes in endothelial dysfunction in the form
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There was a weak positive correlation between urine microalbumin and APACHE-II score in the study population (correlation coefficient $r = 0.199$, $P = 0.166$). However, in a study by Basu et al., among 525 consecutively admitted ICU patients, the urine microalbumin was highly correlated with APACHE II illness severity score reflecting the acute physiologic response to the severe inflammation. The urinary microalbumin was highest among the patients with maximum APACHE II values in a pilot study done on 50 critically ill patients by Mac MacKinnon et al.

The ROC curves showed that the area under the curve for microalbumin in predicting patient mortality was 0.59 (95% CI: 0.41-0.772, $P = 0.398$) and was very close to the null value of 0.5. However, for APACHE II levels, the area under ROC curve in predicting mortality was 0.678 (95% CI: 0.48-0.87, $P = 0.098$). Likewise, APACHE II had the highest area under the curve (0.78) than ACR2 (0.71) and ACR1 (0.58) in predicting the mortality in a study by Basu et al.

The mean microalbumin level was 25.39 g/dl higher in people who met with mortality, compared to people who survived (95% CI: 43.57-94.37, $P < 0.463$), which was statistically not significant; however, the mean APACHE II score was 14.56 in people with mortality, compared to 10.80 in people who survived (mean difference - 3.75, 95% CI: 0.15-7.34, $P = 0.041$), which was statistically significant. A study by Abid et al., in their analysis of 40 ICU patients reported that the increasing urine ACR in patients had significantly higher mortality rates and correspondingly higher APACHE II and SOFA scores.

One of the limitations of the study was its smaller sample size, which may explain the weaker mortality predictivity of microalbuminuria. There is some evidence suggesting the appreciable role of using microalbuminuria as a simple, rapid, inexpensive biochemical tool. A systematic review by Gopal et al., on the ability of urinary microalbumin in predicting the severity of illness among critically ill patients concluded that currently, there was no evidence to suggest use of the test in ICUs and that there was a need to assess the optimal timing and threshold reference value for the urine ACR in diverse, heterogeneous ICU patients.

Implications

The ICU prognostic scores such as APACHE II and the SAP II scores, though useful are very cumbersome tools in day to day practice. Whereas microalbuminuria expressed as ACR is a simple, validated, reliable, inexpensive test that obviates the need for a timed urine collection and
can be performed at the patient’s bedside and results can be obtained within 15 min. Microalbuminuria could be an ideal tool for the early and accurate identification of patients with high risk of morbidity and mortality in ICU thereby guiding the intensivist to optimize triage, judicial allocation of resources and finance, counseling the family, early aggressive life support, and better patient outcome.

CONCLUSION

To conclude, the findings reveal that microalbuminuria weakly correlated with the mortality of the ICU patients and that the APACHE II scores may be more reliable and accurate measure, though it employs cumbersome data collection methods and complex statistical analysis. However, further studies among larger groups of diverse patient categories may help us to confirm the validity gap between urine microalbumin and APACHE II score.

REFERENCES


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Analysis of Factors Affecting Return to Sports after Anterior Cruciate Ligament Reconstruction: A Prospective Clinical Investigation

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Abstract

Introduction: Anterior cruciate ligament (ACL) is the most common ligament injury around the knee. The purpose of ACL reconstruction (ACLR) among sports person is to return athletes to their pre-injury activity level. Even after successful reconstruction, a good number of patients are not able to return to pre-injury status. Hence, it is important to understand the variables influencing return to sports (RTSs). The purpose of this study was to report on the variables proposed to be associated with RTSs following ACLR.

Methods: A total of 100 patients were included in the study. The inclusion criteria were unilateral ACL injury, age between 15 and 45 years, and pre-injury Tegner activity score of 5 or more. Patients with Grade III-IV chondral damage and significant associated ligament injury were excluded from the study. ACLR was done with quadruple hamstring graft. The final results were evaluated by using different knee scores and Tampa Scale for Kinesophobia (TSK) after 1 year.

Results: There was a significant improvement shown by all knee scores. Nearly, 55% were able to return to their pre-injury sports at the same level, 35% shifted to a lower activity level, while the remaining 10% were unable to return to their previous sports activities. Marx scale and the TSK demonstrated a significant difference ($P < 0.001$) between patients who “returned” and those who “did not return” to their previous sports.

Conclusion: This study shows that fear of re-injury is a major factor of not returning to pre-injury sports activity. Further study is needed in this aspect.

Key words: Anterior cruciate ligament, Instability, Kinesophobia

INTRODUCTION

Anterior cruciate ligament (ACL) tears are the most commonly reported knee injury in athletes. In the United States, nearly, 300,000 ACL reconstructions (ACLRs) are performed yearly. About 98% of the orthopedic surgeons recommend surgery if patients wish to return to sports (RTSs). However, unfortunately, not all patients RTSs in the same efficacy following ACLR. Most individuals elect to undergo surgical reconstruction following injury to restore knee function and facilitate RTSs participation. The aim of ACLR is to provide the athletes with the best opportunity to return to pre-injury levels of sports participation. Recently, it has been reported that between 8% and 50% of those with ACLR did not return to the same sports after surgery, even with follow-up times of up to 5 years. It is also reported that 70% of the individuals previously involved in contact sports were unable to return to the same sports after surgery. Among those who did return to their prior sports, up to 21% were reported to have returned with major functional limitations that contributed to a reduced level of performance. In a study conducted among the soccer players of the National Football League, it was found that almost 80% returned to competition after ACL injury. However, the performance of players measured by power ratings was reduced by one-third. Similarly, 22% of the athletes in the National Basketball Association did not RTSs after surgery. In those...
who did return, 44% experienced a decrease in efficiency ratings.\textsuperscript{15} It has been suggested that the high incidence of poor RTSs outcomes following ACLR may be due to a lack of standardized RTSs guidelines and incomplete resolution of physical and psychological impairments.\textsuperscript{3,16-18}

From different literatures, it is evident that more than 50% of the sports person were not able to perform their pre-injury sports activity. This leads to an urgency of improved understanding of variables influencing patients’ ability to RTSs. Several factors were published in literature as contributors to post-operative self-reported disability following ACLR. These were the number of injured knee structures,\textsuperscript{19} quadriceps strength,\textsuperscript{16,20,21} knee pain intensity,\textsuperscript{16,21} knee flexion range of motion,\textsuperscript{13} single-leg hop performance,\textsuperscript{19,21} and pain-related fear of movement/re-injury.\textsuperscript{15} It is unclear that whether self-reported knee function influences return to pre-injury levels of sports participation following ACLR. Furthermore, the relative importance of these factors is unknown.

In this prospective investigation, we examine the differences in clinical variables between those who return to pre-injury level of sports participation and those who do not following ACLR 1 year post-surgery. Based on different literatures, we hypothesized that a combination of demographic, knee impairment, functional, and psychosocial measures would differ and discriminate between those who did and did not RTSs.

**METHODS**

This is an institutional-based, observational, prospective study carried out from February 2013 to March 2015, in our institution, after getting permission from the Ethical Committee. All the patients have been counseled about the advantages and disadvantages and complication of the study, and the written consent has been taken. All the patients with Grade III ACL injury of less than 1 year duration were included in this study. The inclusion criteria were unilateral ACL injury, age between 15 and 45 years, and pre-injury Tegner activity score of 5 or more. This age group with a pre-injury Tegner activity level of at least 5 was chosen to include individuals most likely to be involved in sports-related activities. Patients with bilateral knee injury, prior knee ligament injury and/or surgery, and concomitant ligamentous injury greater than Grade I were excluded from the study. The other exclusion criteria were Grade III-IV chondral damage and significant associated ligament injury requiring reconstruction articular cartilage repair procedure performed in conjunction with ACLR. All surgeries were performed by the senior surgeon by quadruple semimembranosus graft with aperture fixation by interference screw. The rehabilitation was conducted for 6 months in our hospital.

**Evaluation**

To document the progression of the patients’ recovery, clinical evaluations were conducted by several knee scores. Subjective and objective assessment was conducted using the International Knee Documentation Committee (IKDC) form. It has been used across a broad range of knee pathologies, including ACL injury and ACLR. It has provided a valid and reliable measurement (intraclass correlation coefficient [ICC] = 0.94). The IKDC contains 10 items related to knee symptoms and physical function. Scores range from 0 to 100, with higher scores indicating less disability. The Tegner activity-level scale has been used to rate their current level of sports participation as well as to recall their pre-injury level of sports participation. The scale has demonstrated an acceptable test-retest reliability (ICC = 0.80) after ACLR. This is an 11-point grading scale. Level 5 was used as a standard in our study as it indicates participation in sports-related activities at the lowest recreational level. Further evaluations were carried out using the Lysholm and Noyes scales. A knee activity rating scale (Marx scale) was also used preoperatively and at final follow-up to measure the patients’ activities.

Knee ligament laxity was measured at 30\textdegree flexion by OSI CA 4000 arthrometer. OSI CA 4000 arthrometer has been shown to provide valid and reliable measurements of anterior knee joint laxity (ICC = 0.91-0.93). The amount of difference of anterior displacement of the tibia in comparison with nonsurgical sides was the anterior knee joint laxity difference.

Isokinetic strength testing was a reliable method of quadriceps strength testing (ICC = 0.81-0.97). The test was performed with isokinetic dynamometer (Biodex Multi-joint system) at speeds of 60, 180, and 300\textdegree/s. The maximum peak torque in flexion and extension and total work and hamstring/quadriceps ratio were calculated. The test was performed at 3, 6, and 12 months after the surgery.

The patient’s psychological profile was measured with the shortened version of the Tampa Scale for Kinesophobia (TSK-11). Scores on the TSK-11 range from 11 to 44 points. The higher scores indicate greater pain-related fear of movement/re-injury. The TSK-11 is a psychometrically stable instrument to assess the fear of movement/re-injury following ACLR as it has good test-retest reliability (ICC = 0.81).

Data were obtained preoperatively and at subsequent follow-ups at 3, 6, and 12 months following the knee reconstruction. Statistical analysis of data obtained was
performed using non-parametric technique with the Mann–Whitney U-test (Wilcoxon rank-sum test) due to the different variables measured between the two groups.

**RESULTS**

A total of 130 patients (sports person) were included in the study. Among them, 100 patients met all the inclusion criteria (60 men, 40 women; mean ± standard deviation age, 22.4 ± 8.6 years). Distribution of different pre-injury sports activity is shown in Table 1. About 90 patients (90%) reported that they had returned to some form of sports or recreational activity since their surgery; however, only 55 (55%) reported returning to pre-injury levels of sports participation, and these were included in the yes RTSs (Y-RTS) group. About 45 patients (45%) reported that they had not returned to their pre-injury level of sports participation and were included in the no RTSs (N-RTS) group. Demographic information for these patients is shown in Table 2. Of those patients reporting in the N-RTS group, 55.56% (25/45) reported fear of re-injury/lack of confidence as a primary reason for not returning to pre-injury levels of sports participation, and knee joint symptoms (pain, swelling, instability, and muscle weakness) collectively accounted for an additional 44.44% (20/45). Pain (7/45 [15.6%]) and muscle weakness (5/45 [11.1%]) were the most frequently reported knee joint symptoms. The distributions of primary reasons for not returning to pre-injury sports participation are shown in Table 3.

**Knee Scores**

Objective IKDC knee scores of normal or near-normal obtained among the 100 patients treated demonstrated a significant improvement ($P < 0.05$) from the pre-operative value of 33-97% at the final follow-up.

Mean Tegner activity score from 100 patients reviewed demonstrated statistically significant difference ($P < 0.05$) from mean 7.2 points pre-injury to 5.5 points on the final follow-up. Mean subjective knee score of 47 points preoperatively improved to 85 points at the final follow-up among the 100 patients treated using the IKDC evaluation form which compared the investigated knee to the patient’s uninjured contralateral knee. Mean Noyes and Lysholm scores, on the other hand, improved from 45 and 50 preoperatively to 88 and 90 on the final follow-up (Figure 1). These improvements in the Noyes and Lysholm scales were noted to be statistically significant ($P < 0.05$).

Comparing the scores obtained by those who “RTSs” against those who “did not return at the same level of sports activity” revealed no significant differences. In the same way, patients who completely ceased participation in sports activity demonstrated no statistically significant difference with those who “RTSs at a lower level” (objective IKDC [$P = 0.35$]; subjective IKDC [$P = 0.20$]; lysholm [$P = 0.38$]; Noyes [$P = 0.054$]; and Tegner [$P = 0.93$]).

**Isokinetic Tests and Computed Analysis**

Isokinetic tests conducted at 60°/s 3 months following surgery demonstrated a decreased quadriceps strength in the Y-RTS group (23% deficit in total extensor work

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### Table 1: Sports activities among patients

<table>
<thead>
<tr>
<th>Sports activity</th>
<th>Number of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Soccer</td>
<td>31</td>
</tr>
<tr>
<td>Running</td>
<td>15</td>
</tr>
<tr>
<td>Cycling</td>
<td>5</td>
</tr>
<tr>
<td>Volleyball</td>
<td>9</td>
</tr>
<tr>
<td>Swimming</td>
<td>15</td>
</tr>
<tr>
<td>Karate</td>
<td>12</td>
</tr>
<tr>
<td>Kabaddi</td>
<td>13</td>
</tr>
</tbody>
</table>

### Table 2: Demographic variable means and distributions for Y-RTS and N-RTS groups

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Y-RTS ($n=55$)</th>
<th>N-RTS ($n=45$)</th>
<th>$P$ value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>20.9±8.3</td>
<td>24.2±8.8</td>
<td>0.066</td>
</tr>
<tr>
<td>Concomitant injuries</td>
<td>0.9±0.8</td>
<td>0.8±0.9</td>
<td>0.533</td>
</tr>
<tr>
<td>Injury to surgery (days)</td>
<td>72.6±57.6</td>
<td>82.4±68.5</td>
<td>0.43</td>
</tr>
<tr>
<td>Pre-injury Tegner score</td>
<td>8.6±1.4</td>
<td>8.2±1.6</td>
<td>0.74</td>
</tr>
<tr>
<td>Post-surgical Tegner score</td>
<td>8.5±1.6</td>
<td>6.6±1.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Surgery to follow-up (weeks)</td>
<td>50.9±3.0</td>
<td>48.5±5.7</td>
<td>0.17</td>
</tr>
</tbody>
</table>

### Table 3: Distribution of self-reported primary reasons for not returning to pre-injury levels of sports participation

<table>
<thead>
<tr>
<th>Primary reason</th>
<th>N-RTS</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain</td>
<td>7</td>
<td>15.6</td>
</tr>
<tr>
<td>Swelling</td>
<td>4</td>
<td>8.87</td>
</tr>
<tr>
<td>Fear of injury or lack of confidence</td>
<td>25</td>
<td>55.56</td>
</tr>
<tr>
<td>Knee instability</td>
<td>4</td>
<td>8.87</td>
</tr>
<tr>
<td>Muscle weakness</td>
<td>5</td>
<td>11.1</td>
</tr>
</tbody>
</table>

---

**Figure 1: Pre- and post-operative distribution of knee score**

in sports activity demonstrated no statistically significant difference with those who “RTSs at a lower level” (objective IKDC [$P = 0.35$]; subjective IKDC [$P = 0.20$]; lysholm [$P = 0.38$]; Noyes [$P = 0.054$]; and Tegner [$P = 0.93$]).
versus 7.3% deficit in total flexor work) and decreased hamstring strength in the N-RTS group (21.3% deficit in total extensor work versus 22.4% deficit in total flexor work). Tests conducted at 60, 180, and 300°/s in extension 1 year postoperatively demonstrated no statistically significant difference between the Y-RTS and N-RTS groups.

Anterior laxity tests performed with computed analysis (OSI) carried out at 3 months, 1 and 2 years from knee reconstruction demonstrated 90% of the 100 patients treated to have less than 3 mm side-to-side difference, 8% with 3-5 mm difference, and 2% to have more than 5 mm difference; no statistically significant difference was noted among the groups (Figure 2).

**RTSs**

On the final follow-up, 55% of the 100 patients were able to return to their pre-injury sports at the same level, 35% shifted to a lower activity level, while the remaining 10% were unable to return to their previous sports activities (Figure 3). Among the patients who were unable to RTSs, five feared re-injury to their reconstructed knee, another two had pain related to chondropathy, one had extension deficit, while two had pain at tibial fixation site (Table 4).

**Knee Activity Rating Scale (Marx Scale)**

In the final follow-up, 35 of the 45 patients who “did not RTSs” had a mean score of 6.71 points (0-16) with only 6.67% (3) obtaining a score ≥15 points. This group of patients reported some difficulty in resuming running, cutting, decelerating, and pivoting activities.

On the other hand, a mean score of 14.03 points (9-16) was documented among 55 patients who “RTSs.” In this group, 54.55% (30) scored ≥15 points as they did not encounter any difficulty doing the same activities. Statistical analysis carried out using the Mann–Whitney U-test demonstrated a significant difference \( (P < 0.001) \) between patients who “returned” and those who “did not return” to their previous sports (Figure 4).

**Psychological Profile**

Data from the psychological questionnaire administered before the surgery demonstrated that 68.9% (31) of the athletes who “did not RTSs” scored ≥40 points. On the other hand, 85.5% (47) of the athletes who “RTSs,” scored ≤15 points. Statistical analysis using the Mann–Whitney U-test revealed a significant difference \( (P < 0.001) \) between these two groups (Figure 5). Athletes who were able to return to previous sports had a mean score of 14.07 while those who changed or completely stopped any sports activity had an average mean score of 38.46 points.
Table 4: Distribution of factors of unable to RTSs

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Number of points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fear of re-injury</td>
<td>5</td>
</tr>
<tr>
<td>Pain due to chondropathy</td>
<td>2</td>
</tr>
<tr>
<td>Extension deficit</td>
<td>1</td>
</tr>
<tr>
<td>Pain at tibial fixation site</td>
<td>2</td>
</tr>
</tbody>
</table>

RTS: Return to sport

Subsequent Surgeries
Two patients presented with persistent clicking and catching during the 1st year post-ACLR. On the second-look arthroscopy, a medial meniscal tear was demonstrated in one case while the other case had a Grade II chondral pathology at the area of the medial femoral condyle. Partial meniscectomy and chondroplasty were done, respectively. At the final follow-up, both patients were able to return to their previous sports.

DISCUSSION
When the ACL is injured, ACLR is usually considered the gold standard of treatment, especially in young active patients. However, it is also necessary to consider various interconnected aspects (anatomy, biomechanics, and psychology) relating to the patients’ athlete, as these can contribute to determine the outcome of the ACLR, which can range from successful to disastrous. For athletes with ACL tear, the outcome of reconstruction becomes more important as expectations of returning to pre-injury activity levels are usually higher. Unfortunately, even with the present techniques in knee reconstruction, successful RTSs cannot be guaranteed. ACLR in athletes is carried out to achieve a stable knee that can enable them to return to their desired activities. Restoration of mechanical restraints is the initial step in achieving knee functional recovery, but factors including the patients’ motivation and willingness to complete the prescribed rehabilitation program may also play a role in influencing the outcome.

The results of our study using the IKDC (objective and subjective), Noyes, and Lysholm demonstrated a significant overall improvement in all the patients. Commonly utilized knee evaluation scales remain as good indicators in evaluating the results of ACLR. However, in certain cases, return to the same level of previous sports after ACLR is not achieved. To identify the possible factors responsible for preventing successful return to previous sports, two additional scales were utilized for this study: The knee activity rating scale (Marx scale) and the TSK.

The Marx scale demonstrated a significant difference (P < 0.001) between athletes who were able to return to previous sports and those who “did not return to any sports.” In this scale, patients were asked about the components of physical function common to different sporting activities, putting more focus in measuring activity rather than health status.

The TSK, on the other hand, focused on factors which included the patients’ commitment, willingness, and interest in resuming pre-injury activity levels. Valuable information extracted from these additional scales can provide the data necessary to go beyond the objective measures available with the standard knee scales. The importance of using these two questionnaires cannot be undermined, especially in cases where good results with IKDC, Lysholm, Tegner, and Noyes scales are obtained and yet the athlete remains unable to resume the previous activity levels.

This investigation demonstrated that only 55% of the athletes were able to resume the same sports activity at the same level following ACLR while the remaining 45% for various reasons decreased their level of activity (35%) or completely ceased sports participation (10%). Further evaluation revealed that 2/10 had persistent pain related to chondropathy and 2/10 at the area of tibial fixation site and the other factors such as fear for new injury 5/10 and strength deficit 1/10 (Table 3). A previous study conducted by Aglietti demonstrated similar results comparable to our findings. Järvinen et al. found in their studies that 53% and 40%, respectively, “RTSs” following knee reconstruction. On the other hand, Nakayama reported a 92% incidence of RTSs among 50 young athletes reviewed. However, in all these studies mentioned, the main focus was on the technique utilized for reconstruction (patellar tendon vs. hamstring tendon) followed by the analysis of outcome using standard knee rating scales. In cases where less satisfactory results were obtained, possible contributory factors were enumerated, but not thoroughly discussed.

Our study emphasizes that ACLR with hamstring graft and restoration of joint stability is just one of the several factors required to facilitate return of athletes to sports. The other important factors include patient selection, pain, patellofemoral dysfunction, and change in lifestyle, rehabilitation as well as concomitant injuries to the joint. Some studies emphasized the importance of early recovery of knee function as a significant determinant of the long-term outcome of reconstructed knees. ACL is rich in nerve supply which is completely lost in reconstructed knee. Hence, proprioception and neuromuscular control is an important determinant that influences the outcome. As a result, a progressive neuromuscular control rehabilitation program should be made mandatory to minimize the risk of injury and to promote the greater chance of successful return to competition.
The most important observation of our study is that the kinesophobia of patients exerts a certain degree of influence in the final outcome of treatment. Morrey et al. demonstrated that significant mood changes throughout rehabilitation may be a contributing factor to poor psychological and physical outcomes.\textsuperscript{41} Furthermore, Pantano et al. emphasized that a variety of psychosocial factors including motivation influence the level of activity following surgical procedures.\textsuperscript{32} The recognition of the variety of factors influencing outcome following ACLR is important, especially when developing a sports-specific post-operative rehabilitation program focused in facilitating the full return of athletes to the previous levels of activity. Although certain weaknesses are evident in this investigation including the relatively low number of patients included per group and the medium term follow-up achieved, the data obtained can be very important in analyzing the rationale behind some athletes inability to RTSs following ACLR.

**CONCLUSION**

Standard knee scales such as IKDC, Lysholm, Noyes, and Tegner remain a valuable tool for evaluating the progression of knee recovery following ACLR. However, we believe that the additional use of the Marx knee activity rating scale and the TSK provide additional data on the patients’ functional capabilities and psychological profile which could be useful in determining the capacity of athletes to resume pre-injury activity level.

This study provides further insight into clinical variables that empirically discriminate between individuals in RTSs groups. Results suggest that the ongoing knee symptoms following ACLR are associated with individuals returning to pre-injury sports participation levels. These potentially modifiable factors represent important targets for rehabilitation. Findings from this study should be considered. In future, longitudinal studies aimed at the development of return-to-sports rehabilitation guidelines and participation criteria are needed.

**REFERENCES**


Retrospective Analysis of Fast-Track Extubation Protocol for Cardiac Surgical Population in Tertiary Care Hospital: A 2 Years’ Experience

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Abstract

Background: Fast-track cardiac anesthesia aims to reduce the extubation time after cardiac surgery. Reduction in extubation time results in massive cost saving in terms of reduction in intensive care unit stay. In this era of health-care cost escalation, this can effectively reduce the burden on health-care system without compromising patient outcome. We here present a retrospective analysis of fast-track extubation protocol followed in our hospital assessed for 2 years.

Materials and Methods: After ethical committee approval, patients were enrolled into study according to specified inclusion criterion. The patients who were included in the study were tried for fast-track extubation according to predefined protocol. If patient could be extubated at the end of 6 h, and without any post-operative complication, it was categorized into success of fast-track protocol.

Results: A total 192 patients were operation upon in our institute between the specified periods. Total 128 patients were identified for inclusion in fast-track protocol. All patients were tried for fast-track extubation according to weaning protocols. 76% of the total patients were male, while mean age was 64.20 ± 9.22. Diabetes was present in 7% of the patients, whereas obesity was present in 53% of the patients. 33% patient had low ejection fraction. Previous myocardial infarction was seen in nearly 20%. The previous stenting was done in 6% of the patients. Nearly 60% of the patients in fast-track criterion underwent off-pump coronary artery bypass grafting (CABG), 0.7% on-pump CABG, 9.3% mitral valve replacement, 6.25% aortic valve replacement, 1.5% patent ductus arteriosus closure, and 18% with atrial septal defect closure. Most common reason for failure for fast tracking is hemodynamic instability (37.5%), whereas respiratory insufficiency was the second most common cause with 31.25% of the people having it. Bleeding complication was a reason in 18.75%, whereas 12.5% have rhythm disturbance as the cause of failure of fast tracking.

Conclusion: Nearly, two-third of the patients who underwent fast tracking could complete the protocol, reducing the health-care cost by equal percentage. With proper patient selection, fast tracking in cardiac surgery is simple and effective tool as a cost saving measure.

Key words: Cardiac surgery, Fast-track anesthesia, Protocol

INTRODUCTION

Fast-track cardiac anesthesia protocol is a perioperative anesthetic management that aims to facilitate tracheal extubation of patients within 1-6 h after cardiac surgery. Most centers consider fast-track extubation up to 8-10 h postoperatively. Health-care costs are rising significantly. With the increasing number of patients subjected to cardiac surgery and less availability of resources is putting burden on the health-care system. There is a need to rationalize the system for efficient use of available resources. Lately, it has been demonstrated that it is safe, cost-effective, and can make efficient utilization of available resources.1,2

In the last 10 years, there is exponential growth in the field of anesthesia, in the form of availability of newer modalities of monitoring, newer medications, and advancement in the knowledge about mechanism of anesthesia. All this
knowledge makes anesthesia practice safer for the patient as well as anesthesiologist. With this added knowledge, it is necessary to avoid the extra burden on resources, so as to have efficient utilization simultaneously keeping the patient in safe hands.

Studies prove that fast-track cardiac anesthesia is safe and can be employed on a vast number of the patient population provided that there is no contraindication. We started the fast-track cardiac anesthesia protocol in our center (Prathima Hospital) in 2015 and completed nearly 190 patients over a period of 1-year in this institution. We retrospectively analyzed the data for the patients during this 1 year in this study; the data were analyzed to assess the impact of fast-track protocol on patient outcome and success of the protocol.

MATERIALS AND METHODS

This single-center study was performed at Prathima Institute of Medical Sciences, a tertiary cardiac care center catering the need of rural population. The study was approved by Ethics Committee of the Hospital. All cardiac surgical patients posted for surgeries were evaluated by primary investigator 1 day before surgery and enrolled into the study according to inclusion and exclusion criterion.

Inclusion Criteria for Fast-Track Anesthesia

Patients scheduled for isolated coronary artery bypass grafting (CABG), off-pump coronary artery bypass, isolated aortic valve replacement (AVR), or combined AVR with one coronary bypass graft, non-complex isolated cardiac surgical procedures (closure of atrial septal defect [ASD] or removal of an atrial myxoma).

Exclusion Criteria for Fast-Track Anesthesia

Physical status class of >3 (according to the American Society of Anesthesiologists Classification).

Patients undergoing reoperation, chronic obstructive pulmonary disease GOLD class ≥2, left ventricular dysfunction, serum creatinine of ≥150 mmol, body mass index of ≥35 kg, emergency operations, and surgical complications necessitating prolonged cardiopulmonary bypass time (CPB) (>150 min).

The criteria were modified according to available resources in the hospital to better suit the need.

Anesthesia Technique

Preoperative medications were continued according to hospital policy. Tablet pantoprazole 40 mg and lorazepam 2 mg were given orally before night. Anesthesia was induced with midazolam 5 mg, fentanyl 7 µg/kg, and propofol 1 mg/kg. Vecuronium 0.2 mg/kg added and patient ventilated with endotracheal tube. Anesthesia maintained with isoflurane, fentanyl 200 µg/h, and propofol.

All anesthetic medications were stopped at the time of skin closure. Cefoperazone and tazobactam were antibiotic continued till 3rd day post-operative. Post-operative pain management protocol consisted of paracetamol 1000 mg QID and tramadol 100 mg TID separated by dose timings.

Operative Technique

Normothermic non-pulsatile flow was used during CPB. According to the surgeon’s preference, cold antegrade crystalloid cardioplegia or warm intermittent antegrade blood cardioplegia was used to induce and maintain cardioplegic arrest. Patients undergoing on-pump procedure received tranexamic acid 1000 mg before and after pump stoppage.

Patients were extubated in fast-track manner if following criteria were met:

1. Stable hemodynamic parameters without pharmacological or mechanical cardiac supports. Systolic blood pressure of >100 mmHg, diastolic blood pressure <90 mmHg
2. Awake and alert patients. Patients can follow orders
3. A stable sinus rhythm on the electrocardiogram without signs of ischemia. Heart rate of <100/min. No atrial fibrillation
4. Normal respiratory function with O₂ saturation of >90% with FiO₂ <50% and arterial pCO₂ level of <50 mmHg on arterial blood gas analysis
5. Blood loss of <50 ml/h via the chest tubes
6. Urine output of >0.5 ml/kg/h
7. Normothermia.

Patients are declared fast track successful when there is no reoperation, no reintubation, and no operative mortality or morbidity (death within 30 days of surgery).

Statistical Analysis

P value considered statistically significant if it is <0.05. All statistical analysis performed using SPSS 17 percentages was drawn.

RESULTS

During the study period of 2-year, 192 patients were operated for different kind of cardiac surgical procedures. Demographic data of the patients have been shown in Table 1.

Nearly 76% of the patients were male, whereas the mean age of the patient was 64.20 ± 9.22. Diabetes was present in 7% of the patients. 33% patient had low ejection fraction. Previous myocardial infarction was seen in nearly 20%. Previous stenting was done in 6% of the patients.
Out of total 192 patients, 128 fulfilled the criterion for fast-track extubation and were included in the study.

Operative parameters are presented in Table 2.

Nearly 60% of the patients in fast-track criterion underwent off-pump CABG, 0.7% on-pump CABG, 9.3% mitral valve replacement, 6.25% AVR, 1.5% patent ductus arteriosus closure, and 18% with ASD closure.

Most common reason for failure for fast tracking is hemodynamic instability (37.5%), whereas respiratory insufficiency was the second most common cause with 31.25% of the people having it. Bleeding complication was a reason in 18.75%, whereas 12.5% have rhythm disturbance as the cause of failure of fast tracking.

**DISCUSSION**

Health-care cost is ever increasing. The issue is more often related to a country where population is more and resources are limited as in India. Every effort to be made for reduction in the cost of health care whenever and wherever possible, so as to penetrate the health-care benefit to the poorest man in society. One of the factors limiting the decrease in cost of cardiac surgery is length of intensive care unit (ICU) stay. If we can reduce the cost of ICU stay without hampering the patient outcome, it is one step ahead toward achieving our goal for health care for all. Our study shows that nearly 66% of our patients could be fast-tracked because of use of simple protocols which could be easily understood by even paramedical staff and easily followed.

Different combination of medications is possible to have early facilitation of extubation. One of the protocols is having the use of regional anesthesia including epidural technique. However, when we see basic aim of fast tracking, i.e., reduction of health-care costs, the aims is offset by the cost of medications and catheters used for epidural anesthesia, and anxiety of doctors regarding epidural hematoma, and increase in pre-anesthesia duration (for putting epidural). Various combinations of inhalational as well as intravenous opioids could be used, as used in different studies.

We used isoflurane over sevoflurane again as a cost cutting measure and found out it to be a good one. We did not find a patient with intraoperative awareness though bispectral index monitoring was not used.

In the remaining 44% of the patients who could not be fast-tracked, most common reasons were hemodynamic instability and respiratory insufficiency (Table 3).

Various other authors also tried to evaluate the efficacy of fast tracking and found out success rate between 50% and 88% depending on study protocols, extubation protocols, and expertise of the system. Patient load is also an important factor which will determine efficacy of the system by improving overall expertise.

The difference between various studies between successes of the fast tracking could be secondary to assessment of the patient in pre-anesthesia clinic, as patient with high risk were excluded from the study at the initial period, reducing the burden on the ICU nurses. This underlies the fact that most important factor for the success of the fast tracking is proper selection of the patients.

Most of the patients from our study were from diverse range of cardiac surgeries in comparison with other studies, which include specifically CABGs. This shows other types of cases such as single valve surgeries, and septal defects also can be easily tackled by fast-track approach.

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**Table 1: Patient profile**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Incidence</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male gender</td>
<td>144</td>
<td>76</td>
</tr>
<tr>
<td>Age</td>
<td>64.20±9.22</td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>88</td>
<td>45</td>
</tr>
<tr>
<td>Hypertension</td>
<td>102</td>
<td>53</td>
</tr>
<tr>
<td>Obesity</td>
<td>14</td>
<td>7.2</td>
</tr>
<tr>
<td>Low ejection fraction (&lt;50)</td>
<td>64</td>
<td>33.3</td>
</tr>
<tr>
<td>Previous myocardal infarction</td>
<td>39</td>
<td>20.31</td>
</tr>
<tr>
<td>Previous PCI</td>
<td>12</td>
<td>6.25</td>
</tr>
</tbody>
</table>

PCI: Percutaneous coronary intervention

**Table 2: Operative parameters**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Total number of cases (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type of surgery</td>
<td></td>
</tr>
<tr>
<td>Off-pump CABG</td>
<td>78 (60)</td>
</tr>
<tr>
<td>On-pump CABG</td>
<td>4 (0.7)</td>
</tr>
<tr>
<td>Mitral valve replacement</td>
<td>12 (9.3)</td>
</tr>
<tr>
<td>Aortic valve replacement</td>
<td>8 (6.25)</td>
</tr>
<tr>
<td>PDA closure</td>
<td>2 (1.5)</td>
</tr>
<tr>
<td>ASD closure</td>
<td>24 (18)</td>
</tr>
<tr>
<td>Mean pump time</td>
<td>52.4±12.44</td>
</tr>
</tbody>
</table>

CABG: Coronary artery bypass grafting, ASD: Atrial septal defect, PDA: Patent ductus arteriosus

**Table 3: Reasons for failure of fast-track cardiac surgical procedures**

<table>
<thead>
<tr>
<th>Reason for not taking fast-track course</th>
<th>Number of patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemodynamic instability</td>
<td>24 (37.5)</td>
</tr>
<tr>
<td>Respiratory insufficiency</td>
<td>20 (31.25)</td>
</tr>
<tr>
<td>Bleeding</td>
<td>12 (18.75)</td>
</tr>
<tr>
<td>Rhythm disturbance</td>
<td>8 (12.5)</td>
</tr>
</tbody>
</table>
CONCLUSION

Fast-track extubation is easily possible in ICUs, have a high success rate and can be applied over a diverse range of cardiac surgical procedures. The main prerequisite is proper selection of the patients. If it is done, health-care cost can be reduced drastically without increasing patient risk.

LIMITATION OF THE STUDY

This study has got several limitations. First, this is single center retrospective study. The second limitation is a lack of adequate power to define the success of fast-track extubation. The third limitation is data were not collected regarding factors affecting the fast-track extubation.

REFERENCES


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Variations in the Shape of Coronoid Process of Indian Adult Dry Human Mandibles

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Abstract

Background: The coronoid process is an excellent bone graft donor in reconstructive surgeries of various craniomaxillofacial deformities. It can also be used as anthropological marker to assess different populations and races.

Materials and Methods: It is a cross-sectional study consisting of 73 dry adult human mandibles. Variations in the shapes were observed, and the photographs were taken.

Results: Three shapes - triangular, hook, and round were observed. Triangular shape was predominant and hook shape was least common. In females, a round shape was the most prevalent. Bilateral symmetry was observed in 73.9%.

Conclusion: The knowledge of the variations in the shapes of coronoid process is helpful while dealing with the conditions such as zygomatico coronoid ankylosis, coronoid hyperplasia, and coronoid bone grafts.

Key words: Coronoid process, Mandible, Variations

INTRODUCTION

The coronoid process of the mandible projects upward and slightly forward as a triangular plate of bone. Its margins and medial surface give attachment to temporalis muscle.¹ The meaning of coronoid process (Greek-Korone) is crown which is a beak-like projection flattened from side to side at the anterosuperior aspect of ramus of the mandible.² Most of the standard textbooks describe coronoid process as flat, triangular process of mandible. Literature shows the variations in the shapes of coronoid process is classified into 3 types as hook, triangular, and rounded.³⁻⁶ The coronoid process can also be used as an anthropological marker in the determination of race.⁷ Clinically, it is important as it is a membranous bone which can be removed intraorally without any functional deficiency and facial disfigurement for reconstruction of orbital floor deformities, alveolar defects, paranasal sinus augmentation, non-union fractures of mandible, osseous defect reconstruction, and other repairing procedures in craniomaxillofacial surgeries.⁸ This study aims to determine the shapes of coronoid process in relation to gender of Indian adult dry mandibles.

MATERIALS AND METHODS

This study is a cross-sectional study with the sample of 73 dry adult human mandibles (44 Male, 29 Female) consisting of 146 (73 right and 73 left) coronoid processes of mandibles. Damaged mandibles at coronoid process were excluded from the study. Sex of the mandible is determined using metric and nonmetric analysis. Bigonial and bicondylar width, flexion on the posterior surface of mandible, chin shape, and gonial eversion were considered in the sex determination (Figure 1). To control for inter-examiner and intra-examiner reliability, all the observations were performed by a single examiner.

OBSERVATIONS AND RESULTS

Three types of coronoid processes were observed.

• Hooked - Tip pointing backward
• Triangular - Tip pointing straight upward
• Rounded - Rounded tip

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Hook shape was observed in 25 (17.12%) sides (Figure 2), triangular shape in 80 (54.7%) sides (Figure 3), and rounded in 41 (28.08%) sides (Figures 4 and 5).

In this study, 73.9% mandibles were showing bilateral symmetry and only 26.02% of mandibles were showing difference in the shapes in both sides (Table 1).

The triangular shape is predominant in males (68.18%) and rounded in females (39.65%). Hook shape is least common type in both male and females (Table 2, Figure 6).

**DISCUSSION**

The variation in mandibular morphology of mammals reflects specialisations for different diets. Omnivorous and carnivorous mammals possess large mandibular coronoid processes, while herbivorous mammals possess smaller coronoid processes. This is correlated with the relative size of the temporalis muscle that forms an attachment to the coronoid process. The role of this muscle attachment in the development of the variation of the coronoid process is unclear. Anthwal *et al.* have done mouse knockout studies and demonstrated the initiation and growth of the coronoid process depends on two independent processes, with...
initiation being intrinsic to the ossifying bone and growth dependent on the extrinsic effect of muscle attachment. A necessary component of the intrinsic patterning is identified as the paired domain transcription factor Pax9. He also demonstrated that Sox9 plays a role independent of chondrogenesis in the growth of the coronoid process in response to muscle interaction.9

The data of this study were compared with other studies. Table 3 shows the comparison of various studies on the shapes of the coronoid process.

Hook shape was highly prevalent in Bangladeshi population, whereas triangular is prevalent in Indians of different regions. Hook shape is least common in all the regions of India including this study. In this study, the order of prevalence from highest to lowest is triangular, rounded and hook which is similar with Pradhan et al., and not matching with Isaac et al., Vipul et al., and Akram et al.6,10,11

This study shows rounded shape is prevalent in females. Whereas other studies show triangular shape most prevalent in females. Akram et al. found hook shape as most prevalent in females of Bangladesh population (Table 4).4

CONCLUSION

The proper knowledge on the morphological shapes of coronoid process is useful for maxillofacial surgeons as it is used in reconstructions of orbital floor deformities, oro maxilla defects, and paranasal augmentation. Along with the other features of the skull these could be used as an anthropological marker to assess different populations and races.

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Lalitha and Sridevi: Variations in the Shapes of Coronoid Process


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Analysis of Refractive Error Pattern in School Children in South Tamil Nadu

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Abstract

Background: Refractive error is one of the avoidable causes of blindness and low vision. It can restrict progress in education, limit career opportunity, and restrict access to information. Hence, it is essential to understand the pattern of refractive error in school children to plan the effective programs to deal with the problem.

Aim: To assess the pattern of the prevalence of refractive error in school going children. To attend the deviation from emmetropic status in the earliest possible time. Early diagnosis and treatment by mass screening and disability limitation were the prima foci of this study.

Materials and Methods: A total of 1000 students were examined from June 2015 to October 2015 in Theni District in South Tamil Nadu, India. Anterior segment examination was conducted with oblique illumination. Uncorrected, presenting and best-corrected visual acuity was assessed in internally illuminated Snellen's vision chart. Extraocular movements and cover tests were performed using torch light, and retinoscopy and subjective refraction were performed in all the children with an auto refractometer. Fundus evaluation was done with a direct ophthalmoscope.

Results: A total of 1000 students were enrolled. Of them, 524 students were male and 476 were female students. Around 54.10% students were emmetropic. Remaining 45.90% were diagnosed to have a refractive error with distribution as follows: Myopic astigmatism 26%, simple myopia 14.7%, simple hyperopia 14.7%, hyperopia with astigmatism 1.1%, and 1.4% were refractive to glasses.

Conclusion: Clinical evidence suggests that refractive error, including amblyopia and strabismus, is common ophthalmic disorders in children. Refractive error, particularly myopia, plays a substantial burden on the individual and on society. Myopia can have a potential negative impact on career choice, ocular health, and sometimes self-esteem. School-age children constitute a particularly vulnerable group, where uncorrected. Refractive error may have a dramatic impact on learning capability and educational potential.

Key words: Disability, Mass screening, Refractive error

INTRODUCTION

Refractive errors are optical defects of the eye wherein the incident parallel rays of light are not brought to a sharp focus by the cornea and the lens onto the light-sensitive layer of the retina.

According to the World Health Organization, 1.2 million children aged between 5 and 15 years are visually impaired because of uncorrected refractive errors.

Children with these problems need to be identified as early as possible because a delay in the treatment can lead to amblyopia.¹ It also has serious social implications for the child in the school.

MATERIALS AND METHODS

A total of 1000 students were examined from June 2015 to October 2015 in Theni District in South Tamil Nadu, India.
Anterior segment examination was conducted with oblique illumination. Uncorrected, presenting and best-corrected visual acuity was assessed in internally illuminated Snellen’s vision chart. Extraocular movements and cover tests were performed using torch light, and retinoscopy and subjective refraction were performed in all the children with an auto refractometer. Fundus evaluation was done with a direct ophthalmoscope.

**Assessment of Refractive Status**

A methodical evaluation of the anterior segment was done with oblique illumination.

- Uncorrected, presenting and best-corrected visual acuity was assessed with internally illuminated Snellen’s vision chart,
- Extraocular movements and cover tests were performed using torch light, and,
- Retinoscopy and subjective refraction were performed in all children with an auto refractometer,
- Detailed posterior segment evaluation was done with a direct ophthalmoscope.

**RESULTS**

This study included 1000 students in Theni District. Of them, 524 students were male and 476 students were female (Chart 1). Because we analyzed school going children, the age group was between 5 and 15 years. 571 students were in the age group of 5-10 years and 429 students were in the age group of 10-15 years (Table 1).

About 54.10% of students were emmetropic, and remaining 45.90% were diagnosed to have refractive error with a distribution as follows: Myopic astigmatism: 26.1%, simple myopia: 14.7%, simple hypermetropia: 1.4%, hypermetropia with astigmatism and mixed astigmatism: 1.1%. Few myopes (1.4%) were refractory to glasses (Table 2 and Chart 2).

These refractive errors were corrected by glass prescription and importance of compliance was explained to the teacher and the student. Refractory cases (1.4%) underwent fundus examination to look into the other causes of retarded visual acuity,

**DISCUSSION**

- The results of this study are on a high note to the study carried out by Sethi and Kartha (2003). A study of the prevalence of refractive errors in school children aged between 12 and 17 years was conducted by them in Ahmedabad. The results were that 25.32% of the students included in the study had refractive errors.
- Seema et al. (2004) conducted a similar study on the magnitude of refractive errors in school children in a rural block of Haryana. In this study which included 1265 students 172 (13.6%) children were found to have a visual defect.
• In Prema et al., the results of this study showed that 30.57% of students were identified as having defective vision. Out of which 43.75% are boys and 56.25% are girls. There was a significant difference in their residential area; that is 27.08% were in the rural area, 34.37% were from the urban area, and 38.55% were residing in the semi-urban area. The students and their parents were not aware of complications such as amblyopia which could be caused by uncorrected refractive errors.

CONCLUSION

This study shows that most of the children or the parents are unaware of the refractive errors. Therefore, screening in school and pre-school should be carried out periodically.

• Furthermore, school going children and their parents should be educated about signs and symptoms of refractive errors, ocular hygiene and the risk factors involved in the development of these, and other pathological problems.

• The data support the assumption that vision screening of school children in developing countries could be useful in detecting curable causes of vision problems provided detected at the early stage especially refractive errors by which long-term visual disability could be avoided.

REFERENCES

Feasibility of Single Incision Laparoscopic Appendectomy with Conventional Instruments

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Presently, laparoscopic appendectomy is being widely performed. The technology has now percolated to even government and teaching institutes in our country. The safety and efficacy has been proven in various reports and has become the gold standard now.2,3 The advantages include better diagnostic capability, reduced morbidity, and postoperative disability and early return to work.1-4

There have been various reports where single incision surgery is being performed using special single use disposable ports. There have been reports of modifications to this technique using indigenous ports. Both these technique involve a larger incision on the abdominal fascia. We are presenting a different technique using conventional ports and without increasing the incision on the fascial sheath.

INTRODUCTION

In 1901, Kelling performed the first laparoscopic examination of abdomen. It took more than 80 years before the first laparoscopic appendectomy was performed by Semm in 1983. Laparoscopic appendectomy for acute appendicitis was performed by Schreiber in 1987.1 Since then, there has been a significant change in our understanding and experience with laparoscopy which has been aided by rapid technological advancements. Laparoscopy has rapidly evolved to include natural orifice and single incision surgery.

Presently, laparoscopic appendectomy is being widely performed. The technology has now percolated to even government and teaching institutes in our country. The safety and efficacy has been proven in various reports and has become the gold standard now.2,3 The advantages include better diagnostic capability, reduced morbidity, and postoperative disability and early return to work.1-4

MATERIALS AND METHODS

54 consecutive patients diagnosed as acute or chronic appendicitis were included in the study. All the patients...
have been operated by senior surgeon with 10 or more years of laparoscopic surgery experience. The procedures were performed under general anesthesia. Diagnostic laparoscopy was performed for confirmation, followed by appendectomy. Patients were excluded, if a diagnosis other than appendicitis was established. Insertion of additional ports was documented. Conversion to conventional multiport or open appendectomy excluded the patients from the study.

**Technique**

Conventional reusable laparoscopy instruments were used for the procedure. A 1.5-2 cm single incision was taken along the curve of the umbilicus transversely. In case of small umbilicus the incision was vertical in the umbilicus. Peritoneal access was established using Veress needle. Two conventional reusable 5 mm ports were placed through the same incision but different fascial opening, one below the other. A 5 mm 30° telescope was inserted through one of the ports. An atraumatic Babcock grasper was placed through the other port (Figures 1 and 2).

A general scan of the abdomen was performed followed by examination of the terminal ileum and cecum ascending colon by bowel walk. In female patients, examination of uterus, ovary fallopian tubes, and adnexa was also performed.

In the right iliac fossa close to the base of appendix through a 2 mm stab incision a 2 mm assisting instrument was placed. This assist instrument is a 2 mm grasper or a suture passer. The appendix is grasped and lifted up. The mesoappendix is then coagulated using a bipolar grasper inserted through the umbilical port and then divided using a laparoscopic scissor. Two ports have been placed in umbilicus of which one is for the telescope. This leaves one working port necessitating repeated instrument changes. In multiple steps the mesoappendix is coagulated with bipolar grasper and then divided. The appendix is finally bared up to the base (Figures 3 and 4).
The base of appendix is ligated doubly on the body side and the third ligature is placed on slight away from the second. The ligatures are placed by making a Roeder's knot with No 1 Vicryl on a Knot Pusher. The appendix is then divided between the ligature to avoid contamination. The assisting 2 mm instrument is removed under vision. One of the 5 mm ports are replaced by a 10 mm port and the appendix is caught and removed with a claw forceps through the 10 mm port (Figure 5).

Using the 10mm port makes specimen extraction comfortable and avoids contamination of the wound. Hemostasis is confirmed and the ports withdrawn. About 5 ml 2% Lignocaine mixed with 5 ml 0.5% Bupivacaine is infiltrated in the wound for pain relief. Both 10 m and 5 mm ports are closed with No 1 Vicryl, wound is lavaged and skin closed using 3-0 Nylon (Figures 6 and 7).

RESULTS

54 consecutive patients diagnosed as acute or chronic appendicitis with indication for surgery were studied. Two patients were excluded; of which one was having right pyosalpinx and the other had ileocecal mass. In addition to this; in one patient, the base of appendix had sloughed off. The sloughed off stump was buried with an intracorporeal purse string suture on the cecum by conversion to conventional three port laparoscopy.

Remaining 51 patients underwent successful single incision laparoscopic appendectomy (SILA). There was almost equal male-female distribution and the mean age was 20.39 years. Majority of the patients underwent elective surgery for chronic appendicitis. The mean operative time was 30.49 min. Oral feeds were allowed 6 h after the procedure. Patients for elective surgery for chronic appendicitis were admitted on the day of surgery and discharged the next day. Patients operated for acute appendicitis were discharged once the inflammation had subsided; usually on the 2nd or 3rd day after surgery.

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Figure 5: Doubly ligated stump after appendectomy

Figure 6: Immediately after wound closure. Note stab wound in right flank

Figure 7: Cosmetic appearance on POD 8. Scar of stab incision in R flank is hardly noticeable
No major complications were encountered. One patient had a seroma at incision site which settled with conservative management. One patient had slight sero-purulent discharge from the wound, which was managed with antibiotics (Table 1).

**DISCUSSION**

Understanding of pathophysiology of appendicitis and its management has come a long way since Claudius Amyand performed the first appendectomy in 1736. In 1889, McBurney favored early operative intervention and also devised the muscle splitting incision. In 1983, Semm described the first laparoscopic appendectomy. Now, laparoscopic appendectomy has become commonly available and surgeons are moving toward scarless natural orifice surgery. SILA with minimal scarring is a stepping stone toward the scarless procedure.

Multiple techniques have been described for SILA. There have been descriptions of procedures in which special ports have been used. While there are reports in which special curved instruments along with special ports have been used to perform SILA. Some surgeons have used indigenously modified ports as well. Presently there is no standardized technique for performing SILA.

In most of the described techniques, a transumbilical incision is made and a larger facial incision is made to place the special port. This larger fascial incision is considered to increase the risk for future hernia. Also multiple small 5-10 mm incisions are considered to be less traumatic. In some techniques of SILA (SILA Assisted) another fine instrument placed from another site has been used for retraction. It has been noted that complications are lesser in SILA assisted than in SILA. Also there is increased possibility of wound infection as the specimen comes in contact with the wound.

In order to overcome these shortfalls, we have described this new technique. In this technique, no new expensive single use instruments are needed. We have used existing conventional instruments, thus decreasing the cost. In our technique, there is no need for larger fascial incision or the need to dilate the port. The addition of a fine 2 mm grasper/suture passer significantly improves handling of the appendix as well as decreases sword fighting of instruments within the abdomen. The small stab incision does not need to be sutured and gives a very satisfactory cosmetic appearance. As the specimen is retrieved through the 10 mm port; contamination of the wound with the specimen is avoided. To minimize the possibility of a port site hernia, both 5 and 10 mm fascial openings in the abdomen are closed with No 1 Vicryl.

In SILA, it requires greater degree of skill and coordination. It is a challenging procedure because of crowding of instruments, narrow field of view, and difficulty in retraction. There is a danger of electrosurgical complications as well. In our study, the procedures have been performed by an experienced surgeon, an additional fine assisting instrument is used to aid retraction, and bipolar energy has been used to avoid electrosurgical complications. By adding a fine 2 mm grasper does not change the end cosmetic result, but helps to reduce operative time, increase safety, and surgeon comfort (Figures 6 and 7).

In our study, there were no major complications and a minor wound infection was seen in only one patient. Our results are quite comparable to the meta-analysis done by Rehman and Ahmed of various SILA techniques.

**CONCLUSION**

Presently improved cosmesis and reduced scar are the distinct advantage of SILA. However, the results should be reproducible with other operators as well. There should be clear demonstration of decreased morbidity with safety for widespread acceptance and recommendation for which further study is needed.

**ACKNOWLEDGMENT**

We would like to thank our patients for their unwavering faith in us; our staff for their dedication and our colleagues for healthy criticism and appreciation, without which nothing is possible.

**REFERENCES**


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Abstract

Introduction: Oral submucous fibrosis (OSMF) is a potentially malignant disorder with a multifactorial etiology. Recent studies have shown that there are increased levels of fibrinogen degradation products (FDP) in the plasma of OSMF patients suggesting its possible role in etiopathogenesis.

Purpose: To assess the FDP levels in the plasma of OSMF patients in betel nut chewers and in healthy participants without any habits. To correlate the plasma levels of FDP in various clinical stages of OSMF and their role in the etiopathogenesis of the same. Further to read the significance of plasma FDP if any as a prognostic indicator in betel nut chewers without clinical OSMF.

Materials and Methods: This study included 40 cases of betel nut chewers with OSMF, 30 participants with habit of betel nut chewing, and 30 participants without the habit. All participants were evaluated for plasma FDP levels.

Results: In this study, all the participants with OSMF with habit were found to be FDP positive, there were no FDP positive cases for healthy participants without habit. Among the healthy participants with habit, 3 out of 30 were found to be FDP positive. Comparison of FDP values with clinical stages of 40 OSMF patients showed that the correlation was statistically significant.

Conclusion: About 40 cases of clinico-histopathological proven cases of OSMF were included in the present study. All OSMF cases showed an increased trend in the plasma FDP level which was found to directly correlated with the severity of the disease.

Key words: Fibrin, Fibrinogen, Fibrinogen degradation products, Oral submucous fibrosis

INTRODUCTION

Schwartz(1952)¹ described five Indian women from Kenya with a condition of the oral mucosa including the palate and pillars of the fauces, which he called “atrophia idiopathica (tropica) mucosaoritis,” whereas Joshi (1953)² coined the same condition as oral submucous fibrosis (OSMF); however, plethora of terms are also reported to describe the aforesaid condition which includes “diffuse OSMF,” “idiopathic scleroderma of the mouth,” “idiopathic palatal fibrosis,” “sclerosing stomatitis;” and “juxta-epithelial fibrosis.” Pindborg and Sirsat. (1966)³

According to Pindborg and Sirsat (1966),³ “OSMF is insidious chronic disease affecting any part of the oral cavity and sometimes the pharynx. Although occasionally preceded by and/or associated with vesicle formation, it is always associated with juxta-epithelial inflammatory reaction followed by a fibroelastic change of the lamina propria with epithelial atrophy leading to stiffness of mucosa and causing trismus and inability to eat.”

Although a number of postulates such as areca nut chewing, intake of spicy foods stuffed with chilies, genetic
Predisposition, autoimmune characteristics, nutritional deficiency, and infectious agents have been reported to uncover the pathogenesis of the disease, still the credible etiology remains obscure, and therefore, mandating for extensive research in this field. Recent studies have shown that there are increased levels of fibrinogen degradation products (FDP) in the plasma of OSMF patients suggesting its possible role in etiopathogenesis. With this view in mind, the present study is aimed to assess the FDP levels in the plasma of OSMF patients and their critical role in the etiopathogenesis of the same. Further to read the significance of plasma FDP as a diagnostic tool of OSMF in addition to their being labeled as a prognostic indicator in betel nut chewers without clinical OSMF.

**MATERIALS AND METHODS**

Total 100 participants were included in the study and divided into three groups. Group I: Comprised 40 cases of betel nut chewers with clinically evident OSMF. Group II: Comprised 30 participants with habit of betel nut chewing without OSMF. Group III: Comprised 30 participants without the habit of betel nut chewing and without OSMF. Before conducting the study, ethical committee approval was obtained.

Patients with any bleeding or clotting disorder and collagen diseases were excluded from the present study. A detailed case history of each patient was recorded. Provisional diagnoses of OSMF were made on clinical examination and were then further divided into three groups based on the clinical staging given by Ranganathan et al. (2001)\(^5\)\(^6\).

For confirmation of the provisional diagnosis of OSMF, study participants were subjected to scalpel biopsy and histopathologically examined.

**Collection of Sample**

Under all aseptic conditions, 2 ml of venous blood was withdrawn by venipuncture and collected in a sodium citrate tube. Routine hematological investigations were performed. The tubes were allowed to stand for 1 h at room temperature and then centrifuged at 4000 rpm to separate the plasma. Then, platelet poor plasma (PPP) was prepared by centrifuging the supernatant (plasma) obtained after centrifuge (as above) for 10 min at 3700 rpm. This PPP was quantified for FDP levels.

**Estimation of Plasma FDP**

Plasma FDP was quantified using a diagnostic kit (TULIP XL FDP™)\(^7\), “a quantitative latex slide test for detecting cross-linked FDP in human plasma.” XL FDP slide test for detection of cross-linked fibrin degradation products is based on the principle of agglutination. Agglutination is a positive result indicating D-dimer level above 200 ng/ml. No agglutination is a negative result indicating the absence of clinically significant D-dimer levels in the plasma specimen. Agglutination in the highest plasma dilution corresponds to the approximate amount of D-dimer level in ng/ml.

To calculate D-dimer level in ng/ml in the sample, following formula was used:

\[
\text{D-dimer level (ng/ml)} = 200 \times d
\]

\(d\) = highest dilution of plasma showing agglutination during the semi-quantitative test of the sample.

**Statistical Analysis**

The results will be statistically analyzed using Chi-square test, analysis of variance test, and Kruskal-Wallis test.

**RESULTS**

Plasma FDP levels were detected >200 ng/ml in OSMF patients (Group I), and there are no FDP positive cases for participants without habit and without OSMF (Group III). Among betel nut chewers without clinical evidence of OSMF (Group II), 3 out of 30 were found to be FDP positive (Table 1 and Figure 1).

Comparison of mean plasma FDP levels and various clinical stages of 40 OSMF patients showed a statistically significant increase in the FDP levels with increase in clinical stages\((P = 0.000)\) (Table 2 and Figure 2).

**DISCUSSION**

OSMF is predominantly seen in Asian countries, with a high prevalence in India. Recent epidemiological data indicate that the number of cases of OSMF has increased exponentially from 2,50,000 in 1980 to 20,00,000 cases in 1993 justifying an alarming situation.\(^8\) The reasons for such rapid increase of OSMF may be due to an upsurge in the popularity of commercially available areca nut preparations (pan masala) in India and an increased uptake of such preparation by young people due to easy access, effective price changes, and attractive marketing strategies.\(^9\)

The prodromal symptoms include burning sensation in mouth on consumption of spicy food and appearance of blisters, especially in the palate. As the disease progresses, the oral mucosa becomes blanched and white fibrous bands appear, leading to difficulty in mouth opening.\(^10\)
Although a number of postulates have been proposed in the etiopathogenesis of the OSMF, the exact causative factor(s) remained enigma. In the array of proposed hypothesis, the multifactorial origin of the disease is suggested. The role of local irritants in the form of chili, tobacco, areca nut, spicy food, alcohol, and underlying systemic disease can be speculated in view of the geographical and the ethnic distribution of the disease.

Although there is compelling evidence to implicate the habitual chewing of areca nut with the development of OSMF, there are still some cases where the incidence of OSMF was reported without the habit of areca nut chewing, and at the same time, all areca nut chewers do not necessarily develop OSMF.

Fibrinogen is an acute phase reactant which increases throughout the inflammatory process. The body in response to inflammation produces more fibrinogen and its degradation products. Normally, fibrinogen is converted to fibrin by the enzymatic action of thrombin which splits fibrinopeptides A and B from the molecule, leaving fibrin monomers which, in turn, rapidly polymerize to form insoluble fibrin.

In the fibrinolytic process, fibrinogen is degraded by plasmin to fragments X, Y, A, B, C, D, and E. There are four principal fibrin degradation products called X, Y, D, and E. The most notable subtype of fibrin degradation products is the D-dimer. (Figure 3)

| Table 1: Comparison of FDP status in study groups |
|----------------------------------|-----------|-----------|-----------|
| Groups                           | Number (%) |            | Total     |
|                                  | Positive   | Negative  |           |
| OSMF with habit                  | 40 (100.00)| 0 (0.00)  | 40 (100.00) |
| Participants without habit and   | 0 (0.00)   | 30 (100.00)| 30 (100.00) |
| without OSMF                     | 3 (10.00)  | 27 (90.00) | 30 (100.00) |
| Total                            | 43 (43.00) | 57 (57.00)| 100 (100.00) |

Chi-square=88.984, P=0.000. FDP: Fibrinogen degradation products, OSMF: Oral submucous fibrosis

| Table 2: Comparison of FDP values (ng/ml) with various clinical stages of OSMF patient |
|----------------------------------|-----------|-----------|-----------|
| FDP value                        | Clinical stage | Total     |
|                                  | Stage I    | Stage II  | Stage III |
| 400.00                           | 11 (100.00)| 1 (4.35)  | 0 (0.00)  | 12 (30.00) |
| 800.00                           | 0 (0.00)   | 19 (82.61)| 0 (0.00)  | 19 (47.50) |
| 1600.00                          | 0 (0.00)   | 3 (13.04) | 6 (100.00)| 9 (22.50)  |
| Total                            | 11 (100.00)| 23 (100.00)| 6 (100.00)| 40 (100.00)|

Chi-square=58.264, P=0.000. FDP: Fibrinogen degradation products

Figure 1: Comparison of fibrinogen degradation products status in study groups

Figure 2: Comparison of fibrinogen degradation products values (ng/ml) with various clinical stages of oral submucous fibrosis patients

Figure 3: Formation of fibrinogen degradation products by activation of fibrinolytic and coagulation system
FDP have diverse functions. Fibrinopeptides aim to combat the inflammation while FDP tries to counteract the fibrin-like action of fibrin producing factor (FPF) and thrombin produced in the autocatalytic process. Hence, as the severity of the disease increases, more amount of FPF is produced. Fragment Y and to some level fragment X are identified to generate the anticoagulant effect. However, in OSMF, hemorrhagic manifestations are not encountered. Phatak hence described FDP as molecules immunologically similar to fibrinogen.4

The literature states that increase in levels of FDP is a valuable early diagnostic sign of increased rate of fibrin deposition. Furthermore, fibrinogen metabolism has been related to four F's FDP, fibrin precipitating factor (FPF), increased fibrinogen level, and fibrinogen cryoprecipitability.4

In normal participants, the plasma FDP levels are below the detectable levels. When the levels rise above 200 ng/ml, they are detected in the plasma. Therefore, plasma FDP can be used as a diagnostic aid in suspected OSMF cases without biopsy.

Varieties of FDP assessment kits are available with varying sensitivity and specificity. The present kit was used as it is readily available, easy to use, and cost-effective and has sensitivity and specificity of 100%.7

Phatak4 has suggested that saliva may have a role in the causation of OSMF. In his study of seven OSMF cases, he showed that parotid duct saliva of three patients clotted both the oxalated plasma and fibrinogen suggesting thrombin-like behavior of FPF. When this FPF encounters fibrinous exudates in the oral cavity, it promptly clots the exudate. The body in response to this clotting produces more fibrinogen and its degradation products. He also suggested that an increase in the level of FDP is an early diagnostic sign of an increased rate of fibrin deposition.5

The first objective of our study is to detect plasma FDP in betel nut chewers with and without clinical evidence of OSMF. In the present study, plasma FDP levels were detected in all betel nut chewers (Group I Patients) with OSMF, and this finding is in agreement to the results of the previous study done by Phatak (1984)4, Kosthi and Barpande (2007),12 Gharat et al.(2013),17 and Kiran et al. (2013)13 Hence, the hypothesis of FDP being an early diagnostic sign of fibrin deposition is supported. However, our selection criteria differ from the previous study of Kosthi and Barpande (2007),12 in that we have included participants of betel nut chewers with and without OSMF as betel nut is considered to be the main etiologic factor of OSMF.

Plasma FDPs were detected in 3 out of 30 betel nut chewers without clinical evidence of OSMF (Group II). This could be explained by the fact that they might develop the disease in the later stage of life which might be confirmed in a prospective longitudinal study. Since OSMF is a chronic disease and FDP played an important role in its etiopathogenesis, it can be used as a diagnostic aid in suspected OSMF patients, i.e., before the clinical evidence of OSMF. Second, it would have been useful in educating the patient about his/her present situation.

FDP was not detected in Group III cases, and this finding is in accord with the results of study done by Kosthi and Barpande (2007).12

Our second objective is to correlate the plasma FDP levels in various clinical stages of OSMF patients (Group I). We found that with increase in the clinical stages there is increase in levels of FDP (semi-quantitative assessment), and it was statistically significant, and this is in accordance to the study done by Kosthi and Barpande (2007)12 and Gupta et al. (2014)18

As the plasma FDPs are an early indicator of fibrin deposition, the increase in their level with the increase in clinical stage indicates that there is increased deposition of fibrin in OSMF, leading to a severe condition of the disease.

It is suggested that FPF enters into the submucosal zone of oral mucosa and acts on the diffused fibrinogen, inducing fibrin formation. Such fibrin formation stimulates the fibroblasts producing more collagen as well as production of soluble circulating fibrin monomer in plasma known as FDP.16,19

Further, Richardson et al. (1976)20 stated that the fibrin and fibrin degradation products are chemotactic to leukocyte which stimulates the fibroblastic activity and subsequent deposition of collagen in the submucosal connective tissue. Cytokines and growth factors (transforming growth factor beta-1, platelet-derived growth factor-b, and fibroblast growth factor) produced by leukocytes may promote fibrosis by inducing proliferation of fibroblasts, upregulating collagen synthesis and downregulating collagenase production.21

**CONCLUSION**

About 40 cases of clinico-histopathological proven cases of OSMF were included in the present study to find out the role of plasma FDP in the etiolog of OSMF and their significance in reading the severity of the disease.
From the present study, it could be inferred that plasma FDP has got a direct correlation with the deposition of fibrin in the extracellular matrix of the submucosal tissue. Such deposition stimulates the fibroblasts to produce more collagen leading to excess accumulation of collagen eventually causing OSMF. Such relationship of the FDP value with that of the severity of the disease could be used as a useful tool to measure the prognosis of the disease. Furthermore, plasma FDP can be used as a diagnostic aid in suspected OSMF cases without biopsy.

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Evaluation of Effective Role of Posterior Longitudinal Ligament in Management of Traumatic Spine Injuries

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Abstract

Introduction: Ligaments are fibrous bands or sheets of connective tissue linking two or more bones, cartilages or structures together. The ligaments provide stability to a joint during rest and movement. Excessive movements such as hyperextension or hyperflexion or rotations may be restricted by ligaments. In the spine, the ligament helps to provide structural stability.

Materials and Methods: The study of 32 patients, with acute dorsolumbar and cervical fractures, admitted to hospital was carried out. Thorough clinical assessment in the form of mechanism of injury, inspection and palpation of spinous process, and neurological examination was carried out. Patients were investigated in the form of X-ray, computed tomography (CT) scan, magnetic resonance imaging, and CT scan showed a pattern of bony injury. White and Punjabi criteria were used to identify instability in vertebral column and treated (conservatively/operatively) accordingly. Fractures are classified by McAfee and modified Magerl (AO/Association for the Study of Internal Fixation) classification system.

Results: In our experience of spine fractures, very minor cases can be treated with bed rest and physiotherapy; 30% of lesions can be managed with closed treatment; only 60% will require surgery. Distraction posteriorly requires intact anterior longitudinal ligament (ALL) (to prevent over distraction-anatomical hinge) with or without intact posterior longitudinal ligament (PLL) but for indirect reduction of fracture fragments retroreplaced into spinal canal by ligamentotaxis intact PLL is required. If PLL is ruptured surgeon considered either anterior or posterior approach to directly decompress spinal canal and fusion rather than relying on posterior distraction and fusion alone.

Conclusion: PLL forms important structure stabilizing spine along with ALL and ligamentum flavum and other ligaments, helps in resisting excess of flexion, lateral bending, and spinal rotation to lesser extent. It aids in the indirect reduction of fracture fragments by ligamentotaxis.

Key words: Cervical spine, Intervertebral disc, Ligamentotaxis, Posterior longitudinal ligament, Vertebral column

INTRODUCTION

Ligaments are fibrous bands or sheets of connective tissue linking two or more bones, cartilages or structures together. Ligaments provide stability to a joint during rest and movement. Excessive movements such as hyperextension or hyperflexion or rotations may be restricted by ligaments. In the spine, ligament helps to provide structural stability. There are two primary ligament systems in the spine. (1) The intrasegmental system: Holds individual vertebrae together include the ligamentum flavum, interspinous and intertransverse ligaments. (2) The intersegmental system: Holds many vertebrae together include the anterior longitudinal ligament (ALL) and posterior longitudinal ligament (PLL) and the supraspinous ligaments. PLL is placed on the posterior surface of vertebral bodies in the vertebral canal attached to bodies of C2 up to sacrum. Its smooth glistening fibers are attached to intervertebral discs, lamina of hyaline cartilage and adjacent margins of vertebral bodies and not attached firmly and allow escape of basivertebral veins. At cervical and upper thoracic levels, the ligament is broad and of uniform width but
in the lower thoracic and lumbar levels it is denticulated, narrow over vertebral bodies and broad over discs. Longitudinal ligaments transfer tensile loads from bone to bone and when subjected to large loads in situ failure may occur either within the ligament or in the bone at the point of attachment and may degenerate with age. McAfee introduced the concept of unstable burst fracture where anterior and middle column fail in compression and posterior column is disrupted. This fracture is unstable as posttraumatic kyphosis and neurodeficit may develop and PLL is ruptured. We have analyzed the role of PLL in traumatic spine injuries. 

MATERIALS AND METHODS

The study of 32 patients with acute dorsolumbar and cervical fractures admitted to hospital was carried out. Thorough clinical assessment in the form of mechanism of injury, inspection and palpation of spinous process, and neurological examination not forgetting perineal region was carried out. Patients were investigated in the form of X-ray (anterior-posterior/LAT/shoulder pull/open mouth/swimmer’s view), computed tomography (CT) scan, magnetic resonance imaging (MRI), and CT scan showed a pattern of bony injury like fracture of vertebral body, pedicle, laminae, and retropulsed fragment in vertebral canal. MRI was done with 1.5T machine and in different views (axial, coronal, sagittal) showed the extent of trauma to spinal cord parenchyma, nerve roots, intervertebral discs, cord edema, contusion, and laceration. Integrity of spinal ligaments specifically PLL (best seen on T2 density images) noted and relationship to outcome assessed. White and Punjabi criteria (based on radiological and clinical parameters) were used to identify instability in the vertebral column and treated (conservatively/operatively) accordingly. Fractures are classified by McAfee and modified Magerl (AO/Association for the Study of Internal Fixation) classification system.

Patient Assessment

White and Punjabi criteria of instability were used when stability was still doubtful as shown in Table 1.

Management

Conservative

- Postural reduction, bed rest, bowel bladder care, proper nutrition, ambulatory bracing producing a vector opposite of injury force, analgesics, waterbed and frequent change of position, observation for neurological worsening.
- A stable injury such as compression fracture, posterior element fractures and low energy osteoporotic compression and burst fracture were treated by a standard dose of methyl prednisolone within 48 h of injury and dexamethasone in tapered dose after 48 h of injury.
- Reduction of subluxation/dislocation of the cervical spine was done after Crutchfield tong insertion.

Operative

- Surgery was required in unstable three column injuries and significant neurological deficits examples are fracture dislocations, flexion distraction injuries, and burst fractures with neurological deficits.
- Neurologically intact patients with a compression fracture and burst fractures that have >50% loss of vertebral body height or >30% kyphosis in degenerative lumbar (DL) spine are also consider candidates for surgery.
- Canal compromise >50%, scoliosis (lateral tilt >10°) or posterior ligament rupture, 33 mm interspinous distance on lateral radiograph are other indicators of instability in DL spine.
- The posterior approach is the preferred route when there is a trauma to the thoracic and lumbar spine with neurological lesions. Anterior approach can be used to relieve severe anterior compression. When both

Table 1: White and Punjabi Criteria of instability

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</tr>
<tr>
<td>Posterior element destruction</td>
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</tr>
<tr>
<td>Sagittal plane translation &gt;3.5 mm</td>
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</tr>
<tr>
<td>Sagittal plane rotation &gt;11 degree</td>
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</tr>
<tr>
<td>Positive stretch test</td>
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</tr>
<tr>
<td>Medullary (cord) damage</td>
<td>2</td>
</tr>
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<td>Spinal cord or cauda equine damage</td>
<td>2</td>
</tr>
<tr>
<td>Dangerous loading anticipated total of 5 or more=unstable</td>
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</tr>
<tr>
<td>Lumbar white and Punjabi criteria scoring</td>
<td></td>
</tr>
<tr>
<td>Ant element destroyed</td>
<td>2</td>
</tr>
<tr>
<td>Post element destroyed</td>
<td>2</td>
</tr>
<tr>
<td>Flexion extension X-ray criteria</td>
<td></td>
</tr>
<tr>
<td>Sagittal plane translation &gt;4.5 mm or 15%</td>
<td>2</td>
</tr>
<tr>
<td>Sagittal plane rotation</td>
<td>2</td>
</tr>
<tr>
<td>&gt;15 degree at L1-2, L2-3, L3-4</td>
<td></td>
</tr>
<tr>
<td>&gt;20 degree at L4-5</td>
<td></td>
</tr>
<tr>
<td>&gt;25 degree at L5-S1</td>
<td></td>
</tr>
<tr>
<td>Resting X-ray criteria</td>
<td></td>
</tr>
<tr>
<td>Sagittal plane translation &gt;4.5 mm or 15%</td>
<td>2</td>
</tr>
<tr>
<td>Relative sagittal plane angulation &gt;22 degree</td>
<td>2</td>
</tr>
<tr>
<td>Cauda equina damage</td>
<td>3</td>
</tr>
<tr>
<td>Dangerous loading anticipated</td>
<td>1</td>
</tr>
</tbody>
</table>
approaches are used, there was usual practice to leave a week between the two stages. The first stage should be the nerve decompression and if required bone graft can be used for facet joint fusion.

- Fixation was done using moss Miami pedicle screws and rods, Harrington rod distraction, Steffi plating, Hartshill fixation, anterior decompression, and fusion with cage and bone graft.

RESULT

- The indirect reduction was most successful in PLL intact or assumed to be intact (intact middle column) cases compared to PLL ruptured cases (success rate of 100%).
- Ligamentotaxis was successful more often with moss Miami/Steffi plate compared to H-rod or Hartshill. Thus, better indirect reduction occurred with devices which restore both lordosis and posterior body height, e.g., moss Miami.
- The indirect reduction resulted in large defect of bone stock in 2 cases and hence bone graft by anterior route was done to prevent fatigue fracture of pedicular screws/Hrod construct.
- Attempted indirect reduction for subluxation/dislocation of the cervical spine by Crutchfield tongs and traction resulted in neurological deterioration in 1 case, in which PLL was found ruptured on MRI/intraoperatively and cord/root compression by extruded disc had to be dealt with.
- There was no need of compression/distraction in slice fracture and articular process fracture; rotational correction was more important. Hence, there was no difference in results whether moss Miami or Hartshill was used.
- Most people with spinal cord dysfunction presented with the cord intact. Cord injuries as detected by MRI and intra-operative findings suggest 10 cases of contusions or bruising of the cord, 10 cases of compression injuries having pressure on the cord, 6 cases of laceration or tearing, 2 cases of central cord syndrome, and 4 cases of complete severing.

DISCUSSION

- In our experience of spine fractures, very minor cases can be treated with bed rest and physiotherapy; 30% of lesions can be managed with closed treatment; only 60% will require surgery. This 60% which is a high figure can be explained by the fact that ours is a tertiary reference center where cases which require operative treatment mainly are referred.
- It should be emphasize that no treatment can be implemented safely unless a sufficiently skilled surgical team, sufficiently competent paramedical personnel, and adequate equipment are available.
- Newer imaging techniques have aided the evaluation and treatment of the spine and spinal cord injuries particularly CT (bony) and MRI (particularly PLL and posterior annulus).
- PLL along with posterior aspect of body of vertebra, annulus fibrosus (posterior) forms Dennis middle column which is crucial in determining the stability of spine in fracture spine.
- Distraction posteriorly requires intact ALL (to prevent over distraction-anatomical hinge) with or without intact PLL but for indirect reduction of fracture fragments retrospulsed into spinal canal by ligamentotaxis intact PLL is required. If PLL is ruptured surgeon considered either anterior or posterior approach to directly decompress spinal canal and fusion rather than relying on posterior distraction and fusion alone.
- For ligamentotaxis instrumentation should apply both an extension movement and axial distraction. Harrington rod system tends to produce posterior distraction leading to kyphosis and hence should not be preferred in the lower lumbar spine. The indirect reduction was more successful for fracture DL junction than the lower lumbar spine.
- Intra-operative radiographs to confirm that sagittal plane alignment has been restored without over distraction was done to avoid cord damage. Better is C Arm. Postop CT scan to confirm adequacy of canal restoration was done in few cases only. Failure to achieve adequate canal decompression posteriorly necessitated secondary anterior decompression and strut reconstruction/cage in 16.66% cases.
- Ligamentotaxis only was tried in fresh cases and canal compromise<68% as it has been proved beyond doubt by earlier studies that ligamentotaxis succeeds in fresh cases and with less than 68% canal compromise.
- Better indirect reduction occurred with devices that restored both lordosis and posterior body height, e.g., pedicle screw and rod fixation assembly. If reduction resulted in large defect of bone stock in vertebral body (in 16.66% cases), it was necessary to fill anterior defect with anterior corpectomy and bone graft. This prevented fatigue fracture of pedicular screws/Harrington rod construct. In the case of very comminuted fracture with neurological lesion both AP approaches are required.
- Anterior vertebral body excision and grafting were done primarily or become necessary in certain burst fracture with or without intact PLL which presented late and had >68% canal compromise. In flexion distraction
injuries when the posterior and middle column (including PLL) failed by ligamentous disruption posterior spinal arthrodesis with compression system was used. However, in cases in which middle column (including PLL) was determined to be incapable of preventing retropulsion of bone or disc fragments into spinal canal combined AP approach was used.

**CONCLUSION**

PLL is often adequately visualized on MRI particularly if ruptured and lifted up from posterior aspect of vertebral body. It forms important structure stabilizing spine along with ALL and ligamentum flavum and other ligaments, helps in resisting excess of flexion, lateral bending, and spinal rotation to lesser extent. It aids in the indirect reduction of fracture fragments by ligamentotaxis. Reduction of cervical spine subluxation/dislocation by skeleton traction through Crutchfield tongs should not be tried with ruptured PLL (as disc extrusion may occur causing cord compression). With rupture of PLL evident on MRI anterior decompression and fusion in addition to posterior instrumentation should be strongly considered as it is a strong indicator of instability in traumatic spine injuries which cannot be tackled only by posterior instrumentation. PLL is ruptured most often in unstable burst fractures (compression mechanism), chance fractures (tension) and translational injuries. It fails rarely if ever due to rotation and extension.

**REFERENCES**


**Source of Support:** Nil, **Conflict of Interest:** None declared.
Cutaneous Lesions in Newborn Babies: A Hospital-based Study

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Abstract

Background: Newborns can present with a vast variety of skin lesions. Most of these lesions are physiological, transient, or self-limited and require no therapy. Although a few studies have been done, the results of these studies show differences according to racial and environmental factors.

Objective: To study the hospital-based incidence of neonatal dermatoses during the early neonatal period and to know the clinical pattern of various cutaneous lesions.

Materials and Methods: A total of 250 consecutive neonates delivered at VIMS were examined in a hospital-based study satisfying inclusion and exclusion criteria, cross-sectional study between the period of January 2014 and December 2014.

Results: 96.1% of newborns had one or other skin lesions out of 250 newborns examined. Male: Female ratio was 1.27:1. Skin lesions were commonly seen in full-term neonates. Mongolian spot was seen in 61.8%, milia in 32.4%, jaundice in 10.4%, vernix caseosa in 7.2%, and physiological scaling in 6.4%. Among transient non-infective lesions, erythema toxicum neonatorum (ETN) was the most commonly seen in 36.4%, followed by miliaria in 6.4% and transient pustular melanosis in 6.8%. Cafe-au-lait macule was most commonly birthmark seen in 2% followed by congenital melanocytic nevi in 0.15% and hemangioma in 0.4% of cases.

Conclusion: The hospital-based incidence of neonatal dermatoses was 96.1% without sexual predilection. The physiological and transient skin lesions commonly seen were Mongolian spot, milia, ETN, and physiological scaling. It is important to differentiate them from other more serious skin conditions to avoid anxiety among parents and unnecessary therapeutic interventions. Patterns of neonatal dermatoses may be influenced by racial and geographic factors.

Key words: Neonatal, Physiological, Transient dermatoses

INTRODUCTION

The neonatal period is regarded as first 4 weeks of extrauterine life. The transition from an aqueous atmosphere to a dry one represents a dramatic challenge to the skin of a newborn.

The neonatal skin differs from that of an adult structurally and functionally. The cutaneous barrier function, absorption, and temperature regulation vary depending on maturity. A variety of lesions which may be transient, physiological, or pathological may be present during the neonatal period. However, most of these conditions are benign and self-limiting.

Some of the commonly encountered benign and transient lesions during neonatal period are erythema toxicum neonatorum (ETN), miliaria, physiological desquamation last for first few days of life, and others such as Mongolian spots and hemangiomas may persist for several months. Although harmless, these conditions may cause anxiety and concern among the parents to seek medical advice. Other conditions may be pigmented birthmarks, congenital anomalies, cutaneous signs of internal disease, or a pathological condition such as epidermolysis bullosa.

Correct diagnosis and counseling the parents may relieve the anxiety and mental trauma. It also avoids unnecessary
investigations and medications. Further, the pattern of neonatal dermatoses may vary depending on the race and environmental factors. Although a few studies have been done in India, there is none in this part of the country. Hence, a study was undertaken on this subject.

**MATERIALS AND METHODS**

**Source of Data**

All newborns below 28 days of life admitted in postnatal ward/OPD in VIMS and RC, Bangalore.

a. **Duration of study:** 1 year

b. **Inclusion criteria:** Term neonates <28 days of life of either Inborn/OPD will be included in the study.

c. **Exclusion criteria:**
   1. Neonates above 28 days of life.
   2. Preterm neonates
   3. Neonates born to mothers with a history of drug and alcohol abuse, and maternal illness.
   5. Critically sick neonates on ventilator.

**Procedure**

Data were collected after obtaining informed consent from parent/guardian of each neonate up to 28 days of extrauterine life. Detailed history regarding the age of the mother, parity, history of consanguinity, mode of delivery, blood group of mother, and history of maternal illness during pregnancy was taken.

The neonates were examined thoroughly, and the morphology of skin lesions and findings were recorded. The sex, birth weight, presence of any systemic illness, and age at the time of examination were noted in each case. Diagnosis was made based on clinical features. When necessary, Gram’s stains, KOH mount, bacterial culture, and maternal blood venereal disease research laboratory was done.

**Statistical Analysis**

The results of the study were tabulated and analyzed with SPSS 16.0 version. Simple proportions and percentages for incidence, comparison of different variables such as age and sex was used. The relationship between skin lesions and various maternal-neonatal aspects were calculated using Fisher’s exact test and Chi-square test was used, with \( P \leq 0.05 \) considered statistically significant.

**RESULTS**

In the present study, a total number of babies taken as per inclusion and exclusion criteria, out of 260 babies examined taking prevalence into consideration, 250 term newborns had cutaneous lesions (96.1%); 139 (55.56%) were male, 111 (44.4%) were female. Of these, history of consanguinity was present in 8 (3.2%) cases. 229 (91.6%) mothers had undergone regular antenatal checkups.

131 (52.4%) newborns were delivered by normal vaginal route and 119 (47.6%) by cesarean section. 123 (49.3%) mothers were in the age group of 25-30 years, 111 (44.4%) were in the age group of 21-25 years, and 10 (4%) were more than 30 years and below 20 years 6 (2.4%).

Physiological skin lesions found among all babies summoned to 271, followed by transient cutaneous lesions seen in 124, birthmarks in 15, and others in 2. Among the physiological skin lesions, Mongolian spot was the most commonly seen in 154 neonates (61.6%), ETN in 91 (36.4%), milia in 81 (32.4%), physiological jaundice in 26 (10.4%), vernix caseosa in 18 (7.2%), transient pustular lesions in 17 (6.8%), and physiological desquamation in 6 (6.4%).

Distribution of various dermatoses with respect to both sexes.

All cutaneous newborn lesions were more common in males than females except for infantile pustulosis and physiological desquamation, milia which are commonly seen in females (Figures 1-13 and Tables 1-6).

**DISCUSSION**

Cutaneous lesions are not uncommon among neonates. The incidence and pattern of lesions may depend on various factors. In our study, 250 neonates had cutaneous lesions with hospital-based incidence of 96.1%. In a study done in North India, 94.8% neonates had one or more cutaneous lesions.\(^1\)

The prevalence of neonatal dermatoses in different studies varied in between 57% and 99.3%. These differences in the results may be related to study methods and racial factors.\(^2\)

The prevalence of ETN, Milia, and ETN is similar to other Indian studies. The frequency of various neonatal dermatoses in our study is compared with other Indian studies.

The most common skin manifestation noted was Mongolian spots in 154 neonates (61.6%). The incidence of Mongolian spots in our study was similar to others, which ranged from 56% to 98% in various studies of Sachdeva et al.\(^1,3,4\) Its incidence in Asiatic newborn was found to be 81% in one study. Majority were found over lumbosacral region. It is evident that greater the degree of natural pigmentation, the higher is the occurrence of Mongolian
Sandeep, et al.: Cutaneous Lesions in Newborn Babies

Figure 1: Clinical image

Figure 2: Clinical Image

Figure 3: Clinical image

Figure 4: Clinical image

Figure 5: Clinical image
spots in the newborn. Higher incidence in black babies, Asiatic babies, Ladino babies, and Mongolians point toward its racial variation. These were seen more commonly in males and term babies, with a higher incidence in neonates born to multiparous women. There was no relation to maternal illness or mode of delivery similar to a study by Sachdeva et al.\textsuperscript{1}

Milia were seen in 32.4\% cases. This is comparable to the incidence observed by other Indian workers.\textsuperscript{1,3} A higher
incidence was seen in term babies and in babies weighing more than 2.5 kg, delivered vaginally, which has also been noted by Sachdeva et al.\textsuperscript{1,3}

ETN was seen in 36.4\%, similar to Baruah et al.\textsuperscript{4} All the babies were born at term which is in concurrence with other studies.\textsuperscript{1,3} Most of the babies developed ETN on day 2 or 3. The day of examination (second to fourth day) and onset of ETN showed statistical significance ($P < 0.00$).

Physiological scaling was seen in 9.6\% of cases. The incidence of superficial cutaneous desquamation varied from 7.2-83\% in other studies of Dash et al.\textsuperscript{1,3,4} The incidence varies depending on the day of examination, being more in studies where babies were followed up for more than 5 days. It was more in term and post-term neonates. The day of examination (5-7\textsuperscript{th} day) and onset of physiological desquamation showed statistical significance ($P < 0.00$).

Table 1: Relationship of skin lesions with maternal factors

<table>
<thead>
<tr>
<th>Factors</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>H/O consanguinity</td>
<td></td>
</tr>
<tr>
<td>NC</td>
<td>242 (96.8)</td>
</tr>
<tr>
<td>C</td>
<td>8 (3.2)</td>
</tr>
<tr>
<td>Parity</td>
<td></td>
</tr>
<tr>
<td>Primi</td>
<td>113 (45.2)</td>
</tr>
<tr>
<td>Multi</td>
<td>137 (54.8)</td>
</tr>
<tr>
<td>Route of delivery</td>
<td></td>
</tr>
<tr>
<td>Vaginal delivery</td>
<td>131 (52.4)</td>
</tr>
<tr>
<td>Cesarean section</td>
<td>119 (47.6)</td>
</tr>
<tr>
<td>Maternal blood group</td>
<td></td>
</tr>
<tr>
<td>A+</td>
<td>61 (24.4)</td>
</tr>
<tr>
<td>A-</td>
<td>4 (1.6)</td>
</tr>
<tr>
<td>B+</td>
<td>57 (22.8)</td>
</tr>
<tr>
<td>B-</td>
<td>3 (1.2)</td>
</tr>
<tr>
<td>O+</td>
<td>80 (32)</td>
</tr>
<tr>
<td>O-</td>
<td>4 (1.6)</td>
</tr>
<tr>
<td>AB+</td>
<td>40 (16)</td>
</tr>
<tr>
<td>AB-</td>
<td>1 (0.4)</td>
</tr>
<tr>
<td>Maternal age</td>
<td></td>
</tr>
<tr>
<td>&lt;20</td>
<td>6 (2.4)</td>
</tr>
<tr>
<td>21-25</td>
<td>111 (44.4)</td>
</tr>
<tr>
<td>26-30</td>
<td>123 (49.3)</td>
</tr>
<tr>
<td>&gt;30</td>
<td>10 (4.0)</td>
</tr>
</tbody>
</table>

Table 2: Relationship of skin lesions with neonatal factors

<table>
<thead>
<tr>
<th>Neonatal factors</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>139 (55.6)</td>
</tr>
<tr>
<td>Female</td>
<td>111 (44.4)</td>
</tr>
<tr>
<td>Maturity term</td>
<td>250 (100)</td>
</tr>
<tr>
<td>Birth weight</td>
<td></td>
</tr>
<tr>
<td>&gt;2.5 kg</td>
<td>250</td>
</tr>
</tbody>
</table>

Miliaria was seen in 6.4\% cases. The incidence in other studies varies in between 2.6\% and 9.6\% which may be attributed to climatic variations.\textsuperscript{1,9}

Scrotal hyperpigmentation was seen in 0.4\% neonate. There was no history of maternal illness or drug intake. It was speculated that the variation in genital hyperpigmentation may be related to the differential activation of melanocytes.

Table 3: Distribution of various neonatal dermatoses

<table>
<thead>
<tr>
<th>Skin lesions</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physiological skin lesions</td>
<td></td>
</tr>
<tr>
<td>Vernix caseosa</td>
<td>18 (7.2)</td>
</tr>
<tr>
<td>Physiological scaling</td>
<td>16 (5.4)</td>
</tr>
<tr>
<td>Milia</td>
<td>81 (32.4)</td>
</tr>
<tr>
<td>Epstein pearls</td>
<td>2 (0.8)</td>
</tr>
<tr>
<td>Pigmentary changes due to melanin</td>
<td></td>
</tr>
<tr>
<td>Mongolian spot</td>
<td>154 (61.6)</td>
</tr>
<tr>
<td>Pigmentation other than melanin</td>
<td></td>
</tr>
<tr>
<td>Physiological jaundice</td>
<td>26 (10.4)</td>
</tr>
<tr>
<td>Transient non-infective conditions</td>
<td></td>
</tr>
<tr>
<td>ETN</td>
<td>91 (36.4)</td>
</tr>
<tr>
<td>Miliaria rubra</td>
<td>16 (6.4)</td>
</tr>
<tr>
<td>Transient neonatal pustular melanosis</td>
<td>17 (6.8)</td>
</tr>
</tbody>
</table>

Table 4: Pattern of skin lesions

<table>
<thead>
<tr>
<th>Factors</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physiological skin lesions</td>
<td>271 (108)</td>
</tr>
<tr>
<td>Transient non-infective</td>
<td>124 (49.6)</td>
</tr>
<tr>
<td>Birthmarks</td>
<td>15 (8.8)</td>
</tr>
<tr>
<td>Others</td>
<td>2 (0.8)</td>
</tr>
</tbody>
</table>

Table 5: Frequency of various neonatal dermatoses

<table>
<thead>
<tr>
<th>Skin lesions (%)</th>
<th>Sachdeva, et al.\textsuperscript{1}</th>
<th>Dash, et al.\textsuperscript{1}</th>
<th>Baruah, et al.\textsuperscript{4}</th>
<th>Present study</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mongolian spot</td>
<td>60.2</td>
<td>89</td>
<td>-</td>
<td>61.6</td>
</tr>
<tr>
<td>Erythema neonatorum</td>
<td>21</td>
<td>27</td>
<td>34.8</td>
<td>36.4</td>
</tr>
<tr>
<td>Milia</td>
<td>23.8</td>
<td>13</td>
<td>93</td>
<td>32.4</td>
</tr>
<tr>
<td>Physiological scaling</td>
<td>40</td>
<td>18</td>
<td>40</td>
<td>9.8</td>
</tr>
<tr>
<td>Miliaria</td>
<td>20.6</td>
<td>24</td>
<td>13.2</td>
<td>6.4%</td>
</tr>
</tbody>
</table>
Therefore, racial factors and skin type may be important factors in determining genital pigmentation.6

Cafe-au-lait macules (CALMs) were seen in 2.2% of neonates. A study done in Arab and Israel showed the prevalence of CALMs in 0.48% and 0.11% neonates, respectively.8 When multiple CALMs are present, babies have to be followed up for the development of neurofibroma, in conjunction with family history.

Prenatal teeth were seen in 0.4% neonate. A normal mouth may rarely have precocious dentition, with natal (present at birth) or neonatal (eruption after birth) teeth in the lower incisor position or aberrantly placed; these teeth are shed before the deciduous ones erupt. A study done by Baruah et al. also showed similar results.4

In the present study, 0.1% of congenital melanocytic nevi were observed. A giant congenital melanocytic nevus was present in a baby, involving the entire back with multiple satellite lesions distributed all over the body. Congenital melanocytic nevi in newborns showed a prevalence of 0.4-15.6%, with the highest percentage among non-FAIR babies.10

**CONCLUSION**

The hospital-based incidence of neonatal dermatoses was 96.1% with no sexual predilection. Mongolian spot, milia, vernix caseosa, erythema toxicum, and physiological scaling were the common physiological and transient dermatoses seen.

Genetic, environmental, racial, and various maternal and neonatal factors (maternal age, maternal blood group, consanguinity, regular antenatal checkup, and maturity of the baby) may influence the occurrence of certain skin lesions. Patterns of neonatal dermatoses may vary depending on racial and geographical factors also.

Thus, the study of neonatal skin helps to differentiate benign transient lesions from pathological conditions. Most of the skin lesions in newborn are self-limiting requiring no treatment. Correct diagnosis and counseling the parents may relieve the anxiety and mental trauma.

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Plasma Fibrinogen Levels in Acute Stroke in Tertiary Care Hospital, Warangal

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Abstract

Introduction: In urban India, stroke accounts for 1% mortality of all hospital admissions, 4% in all medical cases, and about 20% in all disorders of the central nervous system. Risk factor for stroke includes diabetes, hypertension, smoking, and hyperlipidemia, and these have been linked to abnormalities of hemorheology and coagulation such as increased fibrinogen.

Materials and Methods: Plasma fibrinogen of 50 consecutive patients presenting with acute stroke admitted in Mahatma Gandhi Memorial Hospital, Warangal from 2014 February to 2015 July and compared with 50 controls not suffering from stroke with matched age, sex, and risk factors (controls).

Results: The mean age in the present series was 58.52 years for cases and 58.52 years for controls. The youngest age was 35 years. The oldest age was 85 years. The maximum numbers of patients were in the age group 60-69.

Conclusion: The present study involved 50 patients and 50 controls. The mean fibrinogen level among cases was 602.77 mg% and mean fibrinogen level among controls was 301.3 mg%, which are statistically significant. Mean fibrinogen levels in ischemic stroke were significantly higher than hemorrhagic stroke.

Key words: Cardiovascular diseases, Fibrinogen, Ischemic stroke

INTRODUCTION

In urban India, stroke accounts for 1% mortality of all hospital admissions, 4% in all medical cases, and about 20% in all disorders of the central nervous system.¹

Risk factor for stroke includes diabetes, hypertension, smoking, and hyperlipidemia, and these have been linked to abnormalities of hemorheology and coagulation such as increased fibrinogen.¹

Most cerebrovascular accidents are manifest by the abrupt onset of focal neurologic deficit as if the patient is “struck by the hand of the God.”²

Stroke is defined as an abrupt neurologic deficit that is attributable to focal vascular cause. Risk factors for stroke are hypertension, diabetes, hyperlipidemia, obesity, smoking, atrial fibrillation, carotid stenosis, myocardial infarction, and atrial myxomas.³

Epidemiological observations indicate that high plasma fibrinogen levels strongly correlate with two major thrombotic complications of atherosclerosis, stroke, and myocardial infarction. Thrombosis is increasingly recognized as a central mechanism in stroke as well as in myocardial infarction. Fibrinogen is involved in events thought to play a major role in thrombosis.³

Fibrinogen is a soluble plasma glycoprotein that consists of three non-identical pairs of polypeptide chains (Aα, Bβ, and γ chains).⁴

In the first phase of thrombus formation, soluble fibrinogen is converted into insoluble fibrin by thrombin. Thrombin cleaves Aα and Bβ chains thereby releasing fibrinopeptides, and these fibrinopeptides initiate a
process, in which fibrin monomers begin to gel. These fibrin monomers polymerize to form fibrin polymers. This process continues, and elongation of polymers causes formation of protofibrils. Once a critical mass of long protofibrils is established, and the protofibrils form lateral contacts with other protofibrils thereby forming fibrin clot. Fibrin clot thereby potentiates formation of thrombosis.

Epidemiological observations indicate that high plasma fibrinogen levels strongly correlate with the frequency of two major thrombotic complications of atherosclerosis, stroke as well as myocardial infarction. Thrombosis is increasingly recognized as a central mechanism in stroke and myocardial infarction, and fibrinogen is believed to be involved in events thought to play a major role in thrombosis. Therefore, elucidation of the relationship between fibrinogen and thrombosis may strengthen the predictive value of this protein and suggest new treatment in the management of stroke.\(^1\)

Hence, this study is designed to investigate the association between plasma fibrinogen levels and acute stroke.

**MATERIALS AND METHODS**

**Source of Data**

Plasma fibrinogen of 50 consecutive patients presenting with acute stroke admitted in Mahatma Gandhi Memorial Hospital, Warangal from 2014 February to 2015 July and compared with 50 controls not suffering from stroke with matched age, sex, and risk factors (controls).

The study will be carried out on 50 consecutive patients admitted in Mahatma Gandhi Memorial Hospital, Warangal with acute stroke within 24 h of the onset of symptoms. Detailed history will be taken to find out the risk factors such as hypertension, diabetes, smoking, and alcohol consumption.

Hypertension will be diagnosed by the Joint National Committee VII criteria. Diabetes will be diagnosed by the American Diabetes Association criteria. Smoking will be recorded in terms of number of cigarette pack-years smoked. Thorough general and systemic examination will be carried out.

In addition to routine investigations as per standard protocol in the evaluation of stroke patient, fasting plasma fibrinogen level is estimated and compared to age-, sex-, and risk factors-matched controls. Patients will be followed up till they are discharged from the hospital. Controls will be included who are not suffering from stroke and are age-, sex-, and risk factors-matched.

**Inclusion Criteria**

Patients presenting with acute stroke within 24 h of the onset of symptoms and patients of acute cerebrovascular accident in whom computed tomography scan shows cerebral infarct or hemorrhage were included in the study.

**Exclusion Criteria**

Patients with evidence of uremia, infection, active hepatic disease, patients who have suffered from myocardial infarction in the past 3 months, patients who have undergone surgery in the past 3 months, pregnancy, patients with high leukocyte count, patients with peripheral vascular disease, patients with chronic atrial fibrillation, and patients with a history of stroke were excluded from the study.

Detailed history, clinical examination, and relevant laboratory investigations were performed as per pro forma both in cases and controls. Fasting plasma fibrinogen was estimated in patients and age-, sex-, and risk factors-matched controls. The plasma fibrinogen was measured quantitatively by the Clauss method. The name of kit used was Dade's Behring fibrinogen estimation kit.

Fibrinogen is a plasma protein, which is converted from a soluble protein to an insoluble polymer by action of thrombin resulting in the formation of fibrin clot.

The thrombin clotting time of dilute plasma is inversely proportional to the fibrinogen concentration of the plasma.

Using this principle, Clauss developed a simple quantitative assay for fibrinogen by measuring the clotting time of dilute plasma when excess thrombin is added. The clotting time obtained is then compared with that of a standardized fibrinogen preparation.

Venous blood is collected in an evacuated siliconized blood collection tube containing 1 volume of 0.11 mol/l of sodium citrate (3.8%) and 9 volumes of whole blood, which is centrifuged for 15 min at relative centrifugal force of 2000 g. The buffer which is provided in the Dade Behring fibrinogen estimation kit is used to prepare 1:10 dilution of patient's plasma sample.

**ASSAY:** 0.2 ml diluted (50 µl) citrated plasma sample is incubated for 1 min then 25 µl of thrombin reagent is added at room temperature, and clotting time is then determined at 37° C centigrade using a coagulation instrument. The fibrinogen concentration is then determined by matching the clotting time from the standard provided and prepared in the Dade Behring fibrinogen estimation kit.
RESULTS

Age Distribution
The mean age in the present series was 58.52 years for cases and 58.52 years for controls. The youngest age was 35 years. The oldest age was 85 years. The maximum numbers of patients were in the age group 60-69 (Table 1).

Sex Distribution
Among 50 patients studied, 62% were male and 38% were female. In this study, male: female ratio is 62:38 (Table 2).

Fibrinogen
In the present study, minimum plasma fibrinogen level among cases was 180 mg/dl and minimum plasma fibrinogen level among controls was 130 mg/dl. In the present study, maximum plasma fibrinogen level among cases was 850 mg/dl and maximum plasma fibrinogen level among controls was 680 mg/dl (Table 3).

In present study among cases, mean fibrinogen levels were higher in ischemic stroke than hemorrhagic stroke, which is statistically significant (Table 4).

DISCUSSION

Fibrinogen
The present study involved 50 patients and 50 controls. The mean fibrinogen level among cases was 602.77 mg% and mean fibrinogen level among controls was 301.3 mg%, which are statistically significant.

Mean fibrinogen levels in ischemic stroke were significantly higher than hemorrhagic stroke.

Mistry et al. in their study involving 56 patients admitted in the hospital within 24 h of onset of symptoms. The levels were found to be raised significantly (531.73±74 mg%) compared to those of the age- and sex-matched control group (445.78±92.28 mg%).

When the levels of plasma fibrinogen in stroke group with one risk factor were compared to those of individuals with comparable control group with same risk factor, a significant difference was observed in hypertensive, smokers, diabetic, and obese stroke groups.

Hazra et al. in their study involving 33 patients with cerebral thrombosis and 30 patients with cerebral hemorrhage admitted within 24 h of onset of stroke concluded that the mean plasma fibrinogen concentration in patients with cerebral thrombosis (378.67 mg/dl) is significantly higher when compared to patients with cerebral hemorrhage (224.4 mg/dl) and in the control group (216.67).

Naryanaswamy, Ravi, and Nagarjun in their study involving 30 patients of ischemic stroke and 20 patients of hemorrhagic stroke within 24 h of onset of stroke concluded that mean fibrinogen levels were significantly raised in cases (411.50+111.56 mg/dl) compared to controls (313.76+71.24 mg/dl).

In all the above studies, the level of fibrinogen in cases is increased when compared to controls which are statistically significant. The present study has given similar results as compared with the above-mentioned studies; variation in the level of fibrinogen in the above studies may be due to:
   i. Variation in ethnicity
   ii. The method of fibrinogen assay
   iii. Age group and sex of the patient selected for the study (Table 5).

Age and Fibrinogen
Lee and Maede have shown that fibrinogen level increases with age. This study also demonstrates an increasing trend of fibrinogen with age.
As age advances, there is change in orientation of gpIIb/IIIa receptor causing decreased fibrinolytic activity which accounts for increased plasma fibrinogen levels as age advances. It is likely that mutation accumulation of plasma fibrinogen plays a significant role in the changes of fibrinogen with age. The increase of variance with age is the product of unrepaired evolutional damage in different levels of organization, and the mutations causes increased fibrinogen levels as age advances.

Sex and Fibrinogen
Lee and Maede have shown males have higher fibrinogen when compared to females. This study has shown that fibrinogen was increased in females than males among cases. In controls, males had higher fibrinogen compared to females, which is statistically significant. Higher fibrinolytic activity in females explained the lower fibrinogen levels in females when compared to males.

Smoking and Fibrinogen
Ernst has demonstrated that smoking is associated with increased plasma fibrinogen levels. This study has shown that among cases, mean plasma fibrinogen levels were increased in smokers when compared to non-smokers. Among smokers, the mean plasma fibrinogen levels were higher in cases when compared to control group. Plasma fibrinogen levels increase with smoking and contribute to stroke. Hence, it can be used to predict the stroke in smokers.

Other studies have demonstrated that in smokers, the plasma fibrinogen is elevated because smoking activates lung macrophages which release IL-1β which increases fibrinogen synthesis.

Smoking decreases fibrinolytic activity. Smoking causes endothelial damage resulting in activation of coagulation system and releases clotting factors.

Hypertension and Fibrinogen
Jain et al. have demonstrated fibrinogen levels are higher in hypertensives. Lee has demonstrated plasma fibrinogen was higher among hypertensives. Mistry et al. study, within stroke group, hypertensive patients had higher fibrinogen than normotensive patients.

In the present study, within stroke group (cases), mean fibrinogen levels are higher in hypertensives than normotensive patients. Both studies show similar results suggestive of hypertension which contribute to an increase in plasma fibrinogen levels in stroke. Hence, in hypertensive patients, it can be used for prediction of stroke. Several plausible mechanisms could explain an observed association between elevated fibrinogen levels and hypertension, which is a relation of fibrinogen to increased viscosity and peripheral vascular resistance. Hyperinsulinemia and insulin resistance are common among hypertensives, and hyperinsulinemia is known to cause decreased fibrinolytic activity, hence increased fibrinogen levels in hypertensives.

Markers of inflammation, such as IL-6 and IL-8, are elevated in hypertension and causes reduced consumption of fibrinogen, thereby contributing to increased plasma fibrinogen in hypertension, increased platelet activation, increased activity of coagulation system, and decreased function of the fibrinolytic system.

Diabetes and Fibrinogen
In this study, diabetics had higher mean fibrinogen levels than non-diabetics in both cases and controls.

In Naryanaswamy, Ravi, Nagarjun study among cases, diabetics had higher fibrinogen levels than in non-diabetics, which was statistically significant. Both studies show similar results suggestive of diabetes which contribute to an increase in plasma fibrinogen levels in stroke; Hence, it can be used for prediction of stroke in diabetics. The exact mechanism of increased fibrinogen levels in diabetics is unknown. Insulin stimulates cholesterol synthesis in smooth muscle cells and macrophages of the arterial walls stimulates the proliferation and migration of smooth muscle cells, which are the possible mechanisms. It also enhances the formation of fibrinogen. Endothelial dysfunction which is common in diabetics, which causes decreased fibrinolytic activity and hence increased plasma fibrinogen levels.

The plasma glucagon concentration is positively related to the plasma fibrinogen concentration. Thus, fibrinogen production is markedly enhanced in diabetic patients, and this alteration is likely to determine the observed hyperfibrinogenemia in these patients. Hyperglucagonemia may contribute to the increased fibrinogen production.

Thus, insulin concentrations (and probably also glucose profiles) may need to be maintained at the lowest attainable
level in type 2 diabetes to prevent increased fibrinogen synthesis and stroke.

**Obesity and Fibrinogen**

Meade⁴ and Ernst and Resch¹³ have shown that obese individuals have higher fibrinogen levels.

In this study, in cases, obese individuals had higher mean fibrinogen levels compared to non-obese individuals.

**CONCLUSION**

The mechanisms underlying increased plasma fibrinogen in patients who are overweight.

There is a positive association between obesity (skinfold thickness), plasma insulin concentration, and hyperinsulinemia, thereby stimulating fibrinogen synthesis.

It is possible that the interaction between obesity and physical inactivity may promote dyslipidemia and increased plasma fibrinogen.

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Computerized Tomography Characterization of Mediastinal Lymph Node Masses with Fine Needle Aspiration Cytology Correlation

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Abstract

Introduction: Lung cancer is the most common cancer among men in developed nations, and generally has a poor prognosis. Metastasis of lung cancer to mediastinal lymph nodes presents with a diagnostic dilemma, and many a time, it may be the only presenting sign for lung cancer.

Materials and Methods: All the participants underwent a computerized tomography (CT) imaging of the thorax using a GE Hispeed FX/II spiral CT scanner. Unenhanced CT imaging was done on all patients, with contiguous 10 mm sections obtained at an interval of 1 cm and scanning time of 3-4 s. The distribution, attenuation, and enhancement characteristics of the lymph nodes were evaluated after an intravenous bolus of ionic/non-ionic contrast. All the patients also underwent fine needle aspiration cytology of the lymph node to ascertain the pathophysiology of mediastinal lymphadenopathy.

Results: A total of 32 participants were finally included in the study. Among the participants aged <39 years, most (42.8%) were having lymphoma. At the same time, in those participants aged >40, all of them were having metastatic lesions of the lungs. Among those who reported dyspnea, 75% of the participants were suffering from a malignant lesion of lung, while 25% had lymphoma. Among those participants who had extra-thoracic lymphadenopathy, 86.6% had metastatic lesion of the lung, with the rest having lymphoma and granulomatous lesion of the lungs. Among the patients with no extra-thoracic lymphadenopathy, the vast majority (76.4%) were suffering from metastatic lesions from the lungs.

Conclusion: It was found that the vast majority of patients presenting with mediastinal lymph node enlargement has an underlying lung malignancy presenting as metastasis. Furthermore, CT scan is a modality with can aid in diagnosis and staging of the lymph node enlargement but it cannot replace the importance of a tissue diagnosis.

Key words: Computerized tomography, Fine needle aspiration cytology, Lung cancer, Mediastinal lymphadenopathy

INTRODUCTION

Lung cancer is the most common cancer among men in developed nations, and generally has a poor prognosis. It accounts for almost 13% of all cancer incidence worldwide and 18% of all cancer deaths. In absolute numbers, the incidence of lung cancer is 1.8 million/year worldwide and results in the death of almost 1.4 million patients.¹ Metastasis to mediastinal lymph nodes presents with a diagnostic dilemma, and many a time, it may be the only presenting sign for lung cancer. Mediastinoscopy or thoracoscopy along with histopathological evaluation has been recommended as diagnostic standards but considering the extensive invasiveness and need for general anesthesia; these investigations are less favored by clinicians and patients.² The invasive nature of these tests has led to a demand for minimally invasive tests with comparable yields.

The advent of modern radiological procedures such as computerized tomography (CT) scan and positron emission tomography (PET) has revolutionized the diagnostic procedures in mediastinal lymphadenopathy. A completely
non-invasive procedure like CT scan alone could yield a sensitivity of around 60% and specificity of more than 80%. Other procedures like endobronchial ultrasound are also among possible candidates to replace invasive tests like mediastinoscopy and thoracoscopy and give an acceptable level of yield with very few adverse events. PET is a better procedure in terms of yield, but the procedure is severely limited when considering the cost of equipment and technical requirements of the imaging. Therefore, PET/CT scan is out of the purview for most centers in developing nations.

In this study, we wanted to study the profile of patients who present with mediastinal lymphadenopathy to a tertiary care medical training institution in South India and assess the efficacy of diagnosing the etiology using CT scan. Furthermore, the radiological properties of the lesions were noted and documented in the study, and attempts were made to decipher its association with etiopathogenesis.

**MATERIALS AND METHODS**

The study was conducted in the Department of Radiodiagnosis of Government Medical College, Calicut, Kerala, India. The medical college is a 2500 bedded quaternary care institute, which receives referral patients from across the state of Kerala, India. The campus also houses an Institute of Chest Diseases, which is a state of the art center for all pulmonary conditions.

The study was done among patients from Internal Medicine, General Surgery, Oncology and Pulmonary Medicine Departments, who were suspected of having thoracic lymphadenopathy through radiographic findings and respiratory complaints.

All the patients satisfying inclusion criteria were approached, and those giving written informed consent were included in the study. All the participants underwent a CT imaging of the thorax, using a GE HiSpeed FX/I spiral CT scanner. Unenhanced CT imaging was done on all patients, with contiguous 10 mm sections obtained at an interval of 1 cm and scanning time of 3-4 s. The distribution, attenuation, and enhancement characteristics of the lymph nodes were evaluated after an intravenous bolus of ionic/non-ionic contrast. Delayed scans and upper abdominal sections were obtained in select participants after case-to-case assessment. Those having glomerular filtration rate of <30 ml/min was excluded from a contrast enhanced CT (CECT) imaging.

All the participants also underwent fine needle aspiration cytology (FNAC) of the lymph node to ascertain the pathophysiology of mediastinal lymphadenopathy. The lymph nodes were sampled using a 22-gauge lumbar puncture needle under CT guidance. Those lymph nodes situated in the middle mediastinal compartment were excluded from FNAC due to difficult access and high risks involved in the procedure.

The study was presented before and approved by the Institutional Ethics Committee of Government Medical College, Calicut, Kerala, India. All the participants that were approached for the study gave their consent, and no significant adverse events were reported during the conduct of the study.

**RESULTS**

A total of 32 participants were finally included in the study. All the participants underwent noncontrast and CECT scan, and 29 participants were subjected to FNAC under CT guidance.

A total of 26 (81.25%) participants had metastatic lesions from the lung as the reason for mediastinal lymphadenopathy. Three (9.3%) had lymphoma, 2 (6.25%) had granulomatous inflammation of the nodes suggestive of tuberculosis, and 1 (3.12%) had reactive hyperplasia of the lymph nodes (Table 1).

The clinical and demographic characteristics of the participants were also assessed in the study. Among the participants aged <39 years, most (42.8%) were having lymphoma. At the same time, in those participants aged >40, all of them were having metastatic lesions of the lungs. Among males, the vast majority (83.3%) of the participants had mediastinal lymphadenopathy secondary to malignant lesions of the lung. Among the two female participants, one (50%) had a metastatic lesion of the lung and another (50%) had granulomatous lymphadenopathy. Among the participants who self-reported the use of tobacco, all were suffering from metastatic lesions from the lungs. Among non-smokers too, the majority (66.6%) were suffering from lung metastasis, followed by lymphoma (16.5%) and granulomatous inflammation (11.1%) (Table 2).

Among those who reported dyspnea, 75% of the participants were suffering from a malignant lesion of lung, while 25% had lymphoma. Among the participants who reported chest pain, 76.4% had metastatic lung lesion, while 17.6% had lymphoma. All the participants who had hemoptysis or hoarseness were having metastatic lesions of the lung. In case of cough, 60% had a malignant lung lesion while 20% had granulomatous lesion and 20% had reactive hyperplasia. Among the participants who had neck
swelling, 60% had metastatic lung lesion and 40% had lymphoma (Table 2).

Radiological features of the affected mediastinal lymph nodes were also studied. Among those who had affected anterosuperior group of lymph nodes, 79.3% were suffering from metastatic lesions of the lung and 10.3% had lymphoma. Among the participants who had enlarged middle mediastinal lymph nodes, 80% had a lung malignancy and 10% had lymphoma. All the participants who had enlarged posterior mediastinal nodes were suffering from metastatic lesions from lung malignancies. Among the participants with confluent nodal morphology, the vast majority (83.3%) had metastasis from lungs. A similar trend was observed in those with discrete nodal morphology, with 75% having a malignant primary of the lungs. Metastatic lesion of the lung was the predominant condition in participants who showed attenuation of <30 HU (87.5%) and also in those who had attenuation of more than 35 HU (80.7%). Metastatic lung lesions were seen maximally in cases of those participants which showed homogeneous contrast enhancement (66.6%), patchy contrast enhancement (94.4%), and also rim enhancement (66.6%) (Table 3).

Among those participants who had extra-thoracic lymphadenopathy, 86.6% had metastatic lesion of the lung, with the rest having lymphoma and granulomatous

### Table 1: Type of mediastinal lymph node lesions, characterised by CT and FNAC

<table>
<thead>
<tr>
<th>Type of lesion on CT scan and FNAC</th>
<th>Number</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Metastatic lesions from lungs</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Small cell carcinoma</td>
<td>8</td>
<td>25.00%</td>
</tr>
<tr>
<td>Adenocarcinoma</td>
<td>3</td>
<td>9.30%</td>
</tr>
<tr>
<td>Squamous cell carcinoma</td>
<td>10</td>
<td>21.25%</td>
</tr>
<tr>
<td>Poorly differentiated carcinoma</td>
<td>5</td>
<td>15.62%</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>3</td>
<td>9.30%</td>
</tr>
<tr>
<td>Granulomatous lesion</td>
<td>2</td>
<td>6.25%</td>
</tr>
<tr>
<td>Reactive hyperplasia</td>
<td>1</td>
<td>3.12%</td>
</tr>
</tbody>
</table>

CT: Computerized tomography, FNAC: Fine needle aspiration cytology

### Table 2: Clinico-demographic characteristics of participants

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Metastatic lesion</th>
<th>Lymphoma</th>
<th>Granulomatous</th>
<th>Reactive</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Up to 39 years</td>
<td>1 (14.2%)</td>
<td>3 (42.8%)</td>
<td>2 (28.5%)</td>
<td>1 (14.2%)</td>
<td>7</td>
</tr>
<tr>
<td>40-59 years</td>
<td>14 (100%)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>14</td>
</tr>
<tr>
<td>60 years and above</td>
<td>11 (100%)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>11</td>
</tr>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>25 (83.3%)</td>
<td>1 (50%)</td>
<td>1 (3.3%)</td>
<td>1 (3.3%)</td>
<td>30</td>
</tr>
<tr>
<td>Female</td>
<td>1 (6.7%)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td><strong>Smoking</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>14 (100%)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>14</td>
</tr>
<tr>
<td>No</td>
<td>12 (66.6%)</td>
<td>3 (16.6%)</td>
<td>2 (11.1%)</td>
<td>1 (5.5%)</td>
<td>18</td>
</tr>
<tr>
<td><strong>Symptoms</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dyspnea</td>
<td>6 (75%)</td>
<td>2 (25%)</td>
<td>0</td>
<td>0</td>
<td>8</td>
</tr>
<tr>
<td>Chest pain</td>
<td>13 (76.4%)</td>
<td>3 (17.6%)</td>
<td>1 (5.8%)</td>
<td>0</td>
<td>17</td>
</tr>
<tr>
<td>Hemoptysis</td>
<td>(76.4%)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>10</td>
</tr>
<tr>
<td>Hoarseness</td>
<td>10 (100%)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>8</td>
</tr>
<tr>
<td>Cough</td>
<td>8 (100%)</td>
<td>0</td>
<td>1 (20%)</td>
<td>1 (20%)</td>
<td>5</td>
</tr>
<tr>
<td>Swelling of neck</td>
<td>3 (60%)</td>
<td>3 (60%)</td>
<td>2 (40%)</td>
<td>0</td>
<td>5</td>
</tr>
</tbody>
</table>

### Table 3: Radiological features of lymph nodal involvement

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Metastatic lesion</th>
<th>Lymphoma</th>
<th>Granulomatous</th>
<th>Reactive</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Lymph nodes involved</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anterosuperior</td>
<td>23 (79.3%)</td>
<td>3 (10.3%)</td>
<td>2 (6.8%)</td>
<td>1 (3.4%)</td>
<td>29</td>
</tr>
<tr>
<td>Middle mediastinal</td>
<td>24 (80%)</td>
<td>3 (10%)</td>
<td>2 (6.6%)</td>
<td>1 (3.3%)</td>
<td>30</td>
</tr>
<tr>
<td>Posterior</td>
<td>4 (100%)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td><strong>Nodal morphology</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Confluent</td>
<td>20 (83.3%)</td>
<td>3 (12.5%)</td>
<td>1 (4.1%)</td>
<td>0</td>
<td>24</td>
</tr>
<tr>
<td>Discrete</td>
<td>6 (75%)</td>
<td>0</td>
<td>1 (12.5%)</td>
<td>1 (12.5%)</td>
<td>8</td>
</tr>
<tr>
<td><strong>Attenuation</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;30 HU</td>
<td>7 (87.5%)</td>
<td>0</td>
<td>1 (12.5%)</td>
<td>0</td>
<td>8</td>
</tr>
<tr>
<td>More than 35 HU</td>
<td>21 (80.7%)</td>
<td>3 (11.5%)</td>
<td>1 (3.8%)</td>
<td>1 (3.8%)</td>
<td>26</td>
</tr>
<tr>
<td><strong>Enhancement</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Homogenous</td>
<td>8 (86.6%)</td>
<td>2 (16.6%)</td>
<td>1 (8.3%)</td>
<td>1 (8.3%)</td>
<td>12</td>
</tr>
<tr>
<td>Patchy irregular</td>
<td>17 (94.4%)</td>
<td>1 (5.6%)</td>
<td>0</td>
<td>0</td>
<td>18</td>
</tr>
<tr>
<td>Rim</td>
<td>2 (86.6%)</td>
<td>0</td>
<td>1 (33.3%)</td>
<td>0</td>
<td>3</td>
</tr>
</tbody>
</table>
lesion of the lungs. Among the patients with no extrathoracic lymphadenopathy, the vast majority (76.4%) were suffering from metastatic lesions from the lungs. Among the participants who had vascular compression from mediastinal lymphadenopathy, 86.6% had metastasis from lungs and the rest had lymphoma as their diagnosis. Only 5 participants had pleural effusion, and of this 80% were having metastatic lesions from lungs, and 20% had lymphoma (Table 4).

**DISCUSSION**

Among all the study participants, 81.25% were having metastatic lesions from the lungs, while the rest had varied diagnosis such as lymphoma, reactive lymphadenopathy, and granulomatous inflammation. The prevalence of malignant lesions of the lung as the cause of mediastinal lymphadenopathy is much more than the figures reported in previous studies. Studies done in Germany\(^6\) and the United States\(^7\) have showed the prevalence ranging from 55% to 65%, but our study has shown the prevalence as high as 81.25%. This may be attributed to the fact that tobacco usage, especially crude forms like beedi or khaini, is on the increase in developing countries like India.

Among the participants aged <40 years, only 14.1% were suffering from metastatic lesions from the lung, while all (100%) of the participants aged 40 or above had lung malignancy. The vast majority of the participants (91.3%) were males, and among the male participants, 83.3% were suffering from metastatic lung malignancy. At the same time, only 50% of the female participants had lung metastasis to lymph nodes. This trend conforms to those seen in studies done across the world, on patients with mediastinal lymph node enlargement.\(^8\) All the participants who reported smoking had metastatic lesions of the lung, while only 66.6% of the non-smokers had a diagnosis of a malignant lesion of the lung. The association of smoking with metastatic lung malignancy has been proven across different settings and is similar to what is observed here.\(^9\)

The CT scan is seen as an alternative to more invasive investigations like thoracoscopy and mediastinoscopy in diagnosing and staging mediastinal lymphadenopathy associated with lung malignancy. The CT scan can be beneficial in avoiding the surgical staging procedure in lung malignancy, in the absence of any demonstrable macroscopic lymph node metastasis.\(^10\) The advent of high-resolution CT and CECT has improved the scope of CT scan in comprehensive evaluation of mediastinal lymph nodes.\(^11\) The PET-CT has been a revolutionary method which improved the accuracy in effectively diagnosing and staging the mediastinal lymph nodes, but the expensive nature of the investigation severely limits its utility, at least in developing nations.\(^12\) However, systematic reviews done by Cochrane has shown that all these imaging modalities can be used as an adjuvant in diagnosis and staging but cannot replace the importance of a tissue diagnosis. Furthermore, the review states that imaging done alone, cannot be used to take management decisions in case of mediastinal lymphadenopathy due to probable lung malignancy.\(^13\)

**CONCLUSION**

It was found that the vast majority of patients presenting with mediastinal lymph node enlargement has an underlying lung malignancy presenting as metastasis. Furthermore, CT scan is a modality with can aid in diagnosis and staging of the lymph node enlargement, but it cannot replace the importance of a tissue diagnosis.

**ACKNOWLEDGMENTS**

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Medical Relief Camps in Flood Disaster-affected Area: Experience in Jammu and Kashmir

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Abstract

Introduction: In September 2014, Jammu and Kashmir region of India was hit by flood disaster. Medical relief camps were set up by the army in the affected area. This study characterizes the epidemiology and clinical data of patients seen in two such camps along with challenges faced in running the camps.

Aim/Purpose: (1) To identify medical needs of the flood-affected population and (2) to identify challenges faced in running a medical relief camp in flood disaster-affected area.

Methods: Medical records were created for all registered patients seen at the two camps which were later analyzed. Interview of the medical staff was taken at the end of each camp to identify the difficulty faced by them in running these camps.

Result and Discussion: In a period of 12 camp days, total 3511 patients registered in the two camps mainly comprising of children, adolescents, and geriatric population. Trauma-related injuries (972), acute respiratory tract infection (1152), and chronic medical illness (590) were mostly seen. Trauma-related injuries decreased and communicable diseases increased with time. Total 632 patients presented with somatic complaints only. 40 medical emergencies were also handled in these camps. Inadequate staff, lack of medicines, lack of triage, and inadequate training in disaster management were the major challenges.

Conclusion: Running a medical relief camp after a flood disaster requires a high level of expertise and resources. National or state level disaster medical assistance teams are required for handling future such camps. Public health education programs can be linked with these camps.

Key words: Disaster, Flood, Relief camps

INTRODUCTION

Disaster has both acute and chronic effects on the physical and mental health of the affected population. In the aftermath of disaster injuries, spread of communicable diseases and worsening of non-communicable diseases is reported in several studies.¹-⁴ In the disaster-affected area, medical camps are run by Government, Army, and NGOs to provide medical relief to the affected population, but there is a lack of publications in India on the functioning of these camps. Through this work, we attempt to give an insight on the types of medical illness seen, services provided and challenges faced in functioning of these camps in India after a flood disaster.

In September 2014, the Jammu and Kashmir region was hit by heavy floods caused by torrential rainfall; nearly 284 people died due to floods. According to the Home Ministry of India, several thousand villages across the state were hit, and 350 villages were submerged. More than 2,00,000 people were rescued, including 87,000 from Srinagar city.⁵,⁶

Medical camps to provide medical relief were set up by the army in the flood-affected area. This study analyses the data collected from two such camps. First camp (FC) was situated at airport adjacent to the helicopter landing area, started on 10th September and was meant mainly to attend to medical needs of people rescued through air sorties; this camp continued for 5 days. The camp consisted of a tent

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with the arrangement of 4 beds for emergency inpatient care. The staff at this camp consisted of one MBBS doctor and two nursing personnel.

The second camp (SC) was started on 12th September. It was situated just adjacent to flood-hit area Rajbagh in Srinagar and provided medical services to the flood-affected population in this area; the camp ran for 7 days. Camp was created using tent adjacent to busy road, and there was no arrangement for inpatient admission. The staff at this camp consisted of two MBBS doctors and 1 pharmacist.

The authors as a part of a disaster relief team from the National Institute of Mental Health and Neurosciences got to work and observe proceedings at both these camps and along with medical care were able to assess the psychosocial needs of patients presenting there and provided psychological first aid.

AIMS AND OBJECTIVES

1. To identify medical needs of the flood-affected population.
2. To identify problems faced in running a medical relief camp in flood disaster-affected area.

Participants and Data

Medical records were created and kept for all patients seen at the two camps. Patients who presented to camps were registered with personal information regarding name, age, and sex. A note of presenting complaints, provisional diagnosis as well as medicine prescribed and intervention done was made. Total 907 patients presented at the FC and 2604 at SC. These medical records were reviewed later for data extraction. Furthermore, interview of the medical personnel was taken at the end of each camp to identify the difficulty faced by them in running these camps.

All patients who were requiring tertiary setup care were given emergency treatment, and then, they were sent to higher centers in Jammu, Chandigarh, and Delhi through air with the help of Indian Air Force (IAF).

Apart from the registered patients, there were many people coming to camp for getting knowledge regarding how to prevent outbreak of infectious disease, vaccination to prevent epidemic outbreak and how to purify drinking water. Free drugs, Bottled water, Chlorine tablets, and masks were also distributed at these camps.

Medical complaints were classified as:

a. Trauma: Include laceration, abrasion, infected wound, contusion, hematoma, sprain, pain, and other effects of injury were classified as trauma.

b. Skin-related problems: Infected skin lesions, rashes with itching were categorized under skin-related problems.

c. Acute respiratory infections and their symptoms and signs were regarded as an acute respiratory problem.

d. GIT-related complaints: Comprising mainly of diarrhea and abdominal cramps.

e. Chronic non-communicable disease: Patients who had chronic conditions such as diabetes, hypertension, hypothyroidism, and asthma were classified as chronic non-communicable disease.

f. Psychiatric illness: Patient with known psychiatric illness before onset of flood.

g. Somatic complaints: Complaints of generalized body ache and headache without any above complaints.

h. Others: Rest which cannot be classified in any above categories comprising mainly of patients that came for a health checkup, especially blood pressure measurement without any history or current problem.

Similar classification was used in tsunami disaster medical relief camp by Korean team in Sri Lanka.5

Inclusion Criteria

1. Only patients who were registered and who had complaints or wanted a checkup in the camp were taken for study. People who came for getting information or for bottled water, chlorine tablets, and masks were not included in study data (Tables 1-4).

RESULTS AND DISCUSSION

FC was functional for 5 days, whereas SC for 7 days comprising of 12 camp days. A total of 3511 patients were registered in the two camps, and all were included in this study. The number of daily patients ranged from 137 to 591, and the average was 293. The male to female ratio was 1.52:1 (Male: 2123 and Females: 1388).

• Major representation of patients was from age group 0-20 years (24.49%) and >50 years (32%). The number of patients gradually decreased with passing days at the FC probably because of a decrease in a number of air sorties with time while the number of patients increased substantially in SC with passing days probably due to the spread of infectious diseases and publicity through word of mouth.

• Total of 972 (27.68%) patients presented with trauma which was mainly caused by cuts in lower limbs because of walking in flood water. Others were due to falls, lifting heavy loads, and falling of houses. Some of the trauma-related patients also comprised significant head injuries needing immediate tertiary care referral, fractures, and infected open wounds.
Severity of trauma-related injuries was more in the FC as compared to SC. Number of trauma cases was more in the initial days and declined thereafter.\textsuperscript{5}

- Total 1152 (32.11\%) of patients presented with acute respiratory tract problems in form of cough, cold, throat pain with or without fever. The percentage was high in children and young adults. Number of cases increased gradually as the camps proceeded.\textsuperscript{6}
- A major proportion 590 (16.80\%) presented with chronic problems such as diabetes, hypertension, hypothyroidism, and asthma. Unfortunately, none of the camps had medicines for these disorders otherwise patient turnout could have been even greater. The patient presented with complaints that their medication is washed out in floods, and they are off drug since a week or two. Many of them had raised blood pressure with headache, raised blood sugar level could be determined only in few because of limited resources. About 10\% of chronic problems consisted of thyroid-related abnormalities and about 2\% of asthma. Study done by Chan and Sondorp has pointed out that chronic medical needs seem to be insufficiently addressed in disaster relief interventions.\textsuperscript{9}
- A substantial number of patients 632 (18.00\%) presented with somatic complaints of body ache and headache with onset after floods. This population mainly represents mental stress manifesting as bodily complaints and the need for psychosocial support for these patients.\textsuperscript{10,11} Only those patients who did not have any prior such complaints and who were not having either trauma, skin lesions, acute respiratory infections, any chronic problem, or fever were kept in this group although such complaints in rest of the patients could also have been aggravated due to stress. Total 21 (59\%) patients seen were having psychiatric illness before onset of flood mostly depression (11) and schizophrenia (7). 15 of them were off drug since the onset of the flood.
- Diarrhea was not found to be as prevalent as other Indian studies.\textsuperscript{12,13} It may be attributed to the climatic condition in Jammu and Kashmir which are cooler than rest of India.\textsuperscript{14}
- Total of 246 (7\%) patients were kept in others category and consisted of all other complaints that cannot be kept in above categories. This group mostly consisted of people without any complaints who came just for check up to ensure they are healthy. This type of illness anxiety behavior was more prevalent in the older aged population.
- People evacuated from flood-affected hospitals were also brought to these camps and consisted of some unstable patients with known diagnosis who were still under treatment with diagnosis of acute pancreatitis (1), recently delivered females with cesarean section (2), puerperal sepsis (1), fracture of femur (1), renal failure (1), spinal injury (1), and 1 patient diagnosed as having left-sided malignant stroke of middle cerebral artery.

### Difficulties Faced

1. There was no supply of antihypertensives, antidiabetic, thyroid- and asthma-related drugs though 561 (16.80\%) patients reported with these complaints.
2. There was shortage of supply of tetanus toxoid; many...
patients reported with cuts and bruises while walking in flood water and they themselves demanded tetanus toxoid injections.

3. Supply of emergency medicines was inadequate. The supply of masks and chlorine tablets was also not adequate as per the population needs.

4. As mentioned above, there were patients who came just for checkup without any complaints. Furthermore, there were many patients who only had non-significant complaints related to acute respiratory infection and small cuts and bruises. These patients consumed valuable consultation time that could have been used for seriously ill patients. All this indicated need of staff for triage. Importance of triage in disaster situation has been highlighted in a number of studies.\(^5\)

5. There was a need of dedicated team for health awareness to educate patient visiting camp as well as in nearby areas with topics such as personal hygiene after floods, reentering flood home, cleanup of flood water, minimum standards for water safety, security, sanitation, and shelter. This could have prevented the spread of infectious disease and eventually could have decreased the daily increase in case load especially at SC.\(^6\)

6. In some patients, there was a need of experienced translator to understand their problems better but translation was mostly done by other patients only.

7. No experts were available only MBBS doctors were running the camp.

8. Because of lack of training in disaster management, there were following wrong practices and wrong messages that were being conveyed to public through health workers like:
   a. Patients and relatives presenting to camps were advised that animal carcases need to be disposed at the earliest to avoid epidemic outbreak while WHO guidelines state that dead bodies do not cause epidemics in the aftermath of disasters.\(^7\)\(^8\)
   b. Belief that mass immunization is necessary to prevent epidemic outbreak. Topical antibiotics were frequently prescribed, and washing wounds with antibiotic solutions were recommended.\(^9\)\(^16\)\(^17\)

9. Finally, there was a lack of manpower to run the camp, especially at SC there were only 2 doctors and 1 pharmacist to attend to more than 500 patients per day. Many patients did not register because of the excessive crowd.

CONCLUSION

Running a medical relief camp after a flood disaster requires a high level of expertise and resources. Mostly, trauma-related injuries, acute respiratory tract infections, and chronic medical illnesses are seen though any medical/ surgical condition or emergencies can present at these camps. Dedicated staff for triage is necessary to avoid waste of resources. Efforts should be made to educate the patient and local public regarding prevention of infectious disease spread, safe drinking water, and sanitation practices apart from treatment. It is advisable that staff should go through the National Policy for Disaster Management and WHO guidelines before starting such camps.\(^16\)\(^17\)\(^19\)

Future Directions

- As India is constantly facing disasters and MBBS doctors are mostly deployed in such camps, there is a need for training in disaster management for doctors as a part of MBBS curriculum. If possible, it will be more useful to post specialist doctors in disaster area for better management of the patient. Alternatively, telemedicine can be used to provide specialist support in disaster-affected area.\(^20\)\(^21\)

- It is also highly recommendable to have a national or state level disaster medical assistance team comprising of trained health professionals consisting of specialist doctors, emergency physicians, nursing personnel, and pharmacists with the required infrastructure to set up an emergency medical relief camp in the disaster hit area.\(^22\)\(^23\) This type of team can be mobilized soon after disaster and can be very effective in providing high-level quality medical care in the disaster-affected area.

Limitations of the Study

Due to an emergency situation and lack of diagnostic investigations facility medical complaints were not coded as per ICD or any other such guidelines.

ACKNOWLEDGMENT

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23. Wisconsin -1 Disaster Medical Assistance Team. Available from: http://www.w1dmat.org/.
Compare the Efficacy of Dexmedetomidine and Tramadol in Preventing Intraoperative Shivering in Patients Undergoing Elective Lower Abdominal Surgeries Under Subarachnoid Block

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Abstract

Background: Shivering is an unpleasant and stressful symptom for the patient undergoing surgery. It occurs as a thermoregulatory response to hypothermia. Shivering obscures intraoperative monitoring. It can be detrimental to patients with low cardiorespiratory reserve as it increases oxygen demand, produces arterial hypoxemia and lactic acidosis.

Aims: To study and compare the effectiveness of dexmedetomidine and tramadol to prevent intraoperative shivering in patients undergoing lower abdominal surgeries under subarachnoid block.

Materials and Methods: A cross-sectional comparative study was conducted in Kilpauk Medical College Hospital and Royapettah Hospital in Department of Anaesthesiology in patients aged between 18 and 50 years belonging to the American Society of Anesthesiologists I and II undergoing elective surgical procedures under subarachnoid block. 80 patients were randomly divided into two groups (n = 40) Group D (dexmedetomidine) and Group T (tramadol). The drugs were infused intravenously 10 min after subarachnoid block. The patients were monitored throughout the procedure.

Results: There was a significant reduction in the incidence of shivering in both tramadol and dexmedetomidine groups. Sedation profile was better with the dexmedetomidine when compared with tramadol.

Conclusion: Both the dexmedetomidine and tramadol were effective in the prevention of post-spinal shivering. Dexmedetomidine had better sedation profile without any respiratory depression and had fewer incidences of nausea and vomiting when compared to Tramadol. Thus, it can be used as a better alternate for shivering prophylaxis for patients undergoing surgeries under regional anesthesia.

Key words: Dexmedetomidine, Sedation, Shivering, Subarachnoid block, Tramadol

INTRODUCTION

Shivering is a very unpleasant and physiologically stressful symptom for the patient undergoing surgery and it occurs in various frequencies as a thermoregulatory response to hypothermia. Shivering obscures intraoperative monitoring like electrocardiogram, SPO₂, blood pressure and also increases the intraocular and intracranial pressures. It can be detrimental to patients with low cardiorespiratory reserve since it increases oxygen demand and consumption, produces arterial hypoxemia and lactic acidosis.¹ Some patients find the accompanying cold sensation to be worsened than the surgical pain. Complications of hypothermia and shivering include Ischemia, increased peripheral vascular resistance, increased myocardial oxygen consumption, increased basal metabolic rate, monitoring artifacts showing aberrant values, delayed drug metabolism, altered mental status, and cardiac arrhythmias.
Various methods are available for the control of shivering during anesthesia. Non-pharmacological methods like electrical heaters and radiant warmers are being used to maintain normothermia. However, this equipment may not be practical in all settings. Drugs such as pethidine (meperidine), tramadol, clonidine, nefopam, and ketamine have been used to prevent/treat shivering during spinal anesthesia. Many drugs have been found effective in controlling shivering but most of them produced significant adverse effects such as nausea, vomiting, and respiratory depression. This study was aimed at finding an alternate drug for control of shivering. Dexmedetomidine (a new drug approved for sedation of critically ill or injured patients in intensive care unit. It produces sedation, anxiolysis, hypnosis, analgesia, sympatholytic and has anti-shivering properties. Since it has lesser side effects than other anti-shivering agents, this study was conducted to elucidate the efficacy of dexmedetomidine in the prevention of shivering.

**Aim**

To study and compare the effectiveness of dexmedetomidine and tramadol in the prevention of intraoperative shivering in patients undergoing lower abdominal surgeries under subarachnoid block (SAB).

**MATERIALS AND METHODS**

A cross-sectional comparative study was conducted in Kilpauk Medical College Hospital and Royapettah Hospital in Department of Anaesthesiology. Institutional Ethics Committee approval and written informed consent were obtained. 80 patients, aged from 18 to 60 years, were assessed under the American Society of Anesthesiologists (ASA) physical status I and II scheduled for elective lower abdominal surgical surgeries under SAB will be enrolled in the study. Inclusion criteria were patients undergoing elective lower abdominal surgeries under SAB, age group between 18 and 60 years belonging to ASA I and II. Exclusion criteria were patient refusal, ASA III and IV, pregnant women, patients who are known to be allergic to study drugs, Raynaud’s syndrome, cardiopulmonary, liver diseases, renal diseases and initial body temperature <36.0 and >37.5. Patients were randomly allotted to one of the two groups using a random list. Group D will receive dexmedetomidine (n = 40) and Group T will receive tramadol (n = 40), 10 min after intrathecal injection, either one of the drugs was infused intravenously. Group D, IV bolus of dexmedetomidine 0.5 mg/kg in 100 ml normal saline over a period of 10 min. Group T, 1 mg/kg tramadol in 100 ml normal saline intravenously. All the patients received supplemental oxygen via face mask during surgery. Patients were monitored throughout the procedure and postoperatively for 24 h.

- Motor block is assessed using a modified Bromage scale
- Sensory block is assessed by the pinprick test
- Shivering is graded on a scale similar to that validated by Tsai and Chu
- Sedation score will be assessed using Ramsay Sedation Scale

Patient’s heart rate, blood pressure, oxygen saturation, and temperature were recorded and incidence of severity of shivering every 5 min until the end of surgery. If the patient’s heart rate falls 20% <baseline injection atropine IV hypotension <20% baseline was treated with injection ephedrine IV and IV fluid bolus. Nausea and vomiting were treated with injection ondansetron 0.1 mg/kg IV was administered. Patients who developed shivering during the study period were excluded from the study.

**Statistical Analysis**

Descriptive statistics was done for all data and was reported in terms of mean values and percentages. Continuous variables were analyzed with the unpaired t-test. Categorical variables were analyzed with Fisher’s exact test. Statistical significance was taken as \( P < 0.05 \). The data were analyzed using SPSS version 16.

**RESULTS**

The majority of the tramadol group patients had mean heart rate ranging from 84.28 to 74.45 between baseline
and 110 min intraoperatively. Similarly, majority of the dexmedetomidine group patients had mean heart rate ranging from 82.63 to 74.00 between baseline and 110 min intraoperatively. The association between the intervention groups and mean heart rate is considered to be not statistically significant since $P > 0.05$ as per two-tail unpaired $t$-test (Table 1).

The majority of the tramadol group patients had a mean arterial pressure ranging from 70.70 mm Hg to 76.88 mm Hg between baseline and 110 min intraoperatively. Similarly, majority of the dexmedetomidine group patients had mean arterial pressure ranging from 72.08 mm Hg to 84.48 mm Hg between baseline and 110 min intraoperatively. The association between the intervention groups and mean arterial pressure is considered to be not statistically significant since $P > 0.05$ as per two-tail unpaired $t$-test (Table 2).

The majority of the tramadol group patients had mean temperature ranging from 36.12°C and 35.90°C between baseline and 110 min intraoperatively. Similarly, majority of the dexmedetomidine group patients had mean temperature ranging from 35.89°C to 36.09°C between baseline and 110 min intraoperatively. The association between the intervention groups and mean temperature is considered to be not statistically significant since $P > 0.05$ as per two-tail unpaired $t$-test (Table 3).

The majority of the tramadol group patients had mean shivering grade ranging from 0.00 to 0.05 between baseline and 65 min intraoperatively. Similarly, majority of the dexmedetomidine group patients had mean shivering grade ranging from 0.00 to 0.05 between baseline and 65 min intraoperatively. The association between the intervention groups and mean shivering is considered to be not statistically significant since $P > 0.05$ as per two-tail unpaired $t$-test (Table 4).

The association between the intervention groups and mean sedation score is considered to be statistically significant from 20 to 100 min since $P < 0.05$ as per unpaired $t$-test. In patients belonging to tramadol intervention group, the mean sedation score is decreased to an average of 1.84 points in comparison with patients belonging to dexmedetomidine intervention group in whom the mean sedation score is an average of 2.67 points. This indicates that there is a true difference among intervention groups, and the difference is significant with a $P$-value of 0.0000 according to unpaired $t$-test. In this study, no patient from tramadol group had bradycardia but three patients from dexmedetomidine group had a fall in heart rate of <60 beats/minute. The $P = 0.067$ that is not statistically significant (Table 5).

### DISCUSSION

Shivering continues to be a common problem faced by the anesthesiologist during intra- and post-operative periods following spinal anesthesia. Unfortunately, there is no gold standard drug or definitive strategy drawn in the
management of this commonly encountered problem. Multiple neurotransmitter pathways have been found to involve in shivering and most of the drugs such as opioids (pethidine and tramadol), doxapram, ketanserin, propofol, ketamine, clonidine, and nefopam used acts on these pathways to control shivering. However, adverse effects such as hypotension, sedation, respiratory depression, nausea, and vomiting limit their use. Hence, this study was undertaken to study and compare the effectiveness of dexmedetomidine and tramadol in the prevention of intraoperative shivering in patients undergoing elective lower abdominal surgeries under spinal anesthesia. Furthermore, in this study, we compared the side effect profile of these drugs. Few studies have attempted to study the correlation between heart rate, mean arterial pressure, temperature, shivering grade, respiratory rate, oxygen saturation and side effect profile of tramadol, normal saline, and other drugs with dexmedetomidine. Usta et al. conducted the study to evaluate the effect of dexmedetomidine on shivering in patients undergoing minor surgical procedures under spinal anesthesia with hyperbaric bupivacaine. In that 60 patients (ASA 1 and 2, aged 18-50 years) were equally divided into two Groups C and D. In that Group D received dexmedetomidine and the Group C received normal saline as placebo. He concluded that dexmedetomidine infusion in the perioperative period significantly reduced the incidence of shivering in patients undergoing minor procedures under spinal anesthesia without any significant adverse effects during the perioperative period.

Fern and Misiran in their study demonstrated that all the three drugs dexmedetomidine, pethidine, and tramadol were effective in treating post-neuraxial anesthesia shivering. Dexmedetomidine appears to be a more effective than pethidine and tramadol (100% vs. 85% vs. 55%, respectively). However, the only significant difference statistically was demonstrated only between dexmedetomidine and tramadol and not between other drugs in reducing post-neuraxial anesthesia shivering. In our study, out of 80 patients 3 patients in dexmedetomidine group and 4 patients in tramadol group developed shivering grade ranging from 2 to 3 which was not statistically significant. In our study, sedation scores in dexmedetomidine group were significantly higher than the baseline values and values in tramadol group which were statistically significant. Most of the patients in dexmedetomidine group achieved the sedation score of 3 and in tramadol group achieved the score of 2. In the study by Bozgeyik et al. showed average sedation score of 3 in dexmedetomidine group which was statistically significant.

Table 3: Comparison of temperature of both groups

<table>
<thead>
<tr>
<th>Time (minutes)</th>
<th>Group T</th>
<th>Group D</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number</td>
<td>Mean±SD</td>
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<tr>
<td>Baseline</td>
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</tr>
<tr>
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<tr>
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<tr>
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<tr>
<td>100</td>
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<td>36.03±0.15</td>
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<tr>
<td>110</td>
<td>40</td>
<td>36.09±0.20</td>
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SD: Standard deviation

Table 4: Comparison of shivering grade of both groups

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<tr>
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</table>

SD: Standard deviation, NA: Not available

Table 5: Comparison of sedation score of both groups

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<th>Group D</th>
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<td>Mean±SD</td>
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</tr>
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<td>0±0</td>
<td>40</td>
</tr>
<tr>
<td>10</td>
<td>40</td>
<td>2±0</td>
<td>40</td>
</tr>
<tr>
<td>20</td>
<td>40</td>
<td>2±0</td>
<td>40</td>
</tr>
<tr>
<td>30</td>
<td>40</td>
<td>2±0</td>
<td>40</td>
</tr>
<tr>
<td>40</td>
<td>40</td>
<td>2.0±0.16</td>
<td>40</td>
</tr>
<tr>
<td>50</td>
<td>40</td>
<td>2.0±0.16</td>
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</tr>
<tr>
<td>60</td>
<td>40</td>
<td>2.0±0.22</td>
<td>40</td>
</tr>
<tr>
<td>70</td>
<td>40</td>
<td>2.0±0.22</td>
<td>40</td>
</tr>
<tr>
<td>80</td>
<td>40</td>
<td>2.08±0.27</td>
<td>40</td>
</tr>
<tr>
<td>90</td>
<td>40</td>
<td>2.08±0.27</td>
<td>40</td>
</tr>
<tr>
<td>100</td>
<td>40</td>
<td>2.08±0.27</td>
<td>40</td>
</tr>
<tr>
<td>110</td>
<td>40</td>
<td>2.0±0.22</td>
<td>40</td>
</tr>
</tbody>
</table>

SD: Standard deviation, NA: Not available
when compared to average score 2 in tramadol group intraoperatively. This sedation score in dexmedetomidine group might have removed anxiety in patients. In our study heart rate, blood pressure, respiratory rate, oxygen saturation, and side effect profile were not statistically significant. This observation was confirmed by similar findings in the study by Iqbal et al. stating no significant difference in these variables between the study drugs. Iqbal et al. in their study compared granisetron with meperidine.

CONCLUSION

In our study, both the dexmedetomidine and tramadol were effective in the prevention of post spinal shivering. Dexmedetomidine had better sedation profile without any respiratory depression and had fewer incidences of nausea and vomiting when compared to tramadol. Hence, it can be used as a better alternate for shivering prophylaxis in patients undergoing surgeries under regional anesthesia.

REFERENCES

Single Surgeon’s Experience of Laparoscopic Cholecystectomies Performed at Teaching Hospital for more Than Four Years: A Retrospective Study

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Abstract

Introduction: Laparoscopic cholecystectomy is one of the most commonly performed surgery and now this is the gold standard for the treatment of gallstone disease. With the advancement of time and sharing of the surgical experiences, its surgical outcomes are improving drastically.

Purpose: The aim of this study is to share the experience and lesson learnt from the series of this commonly performed surgery of laparoscopic cholecystectomy to improve it further in coming future.

Materials and Methods: Data from the record of all cases of laparoscopic cholecystectomies performed by the main author himself during the period from 1 November, 2011, to 30 April, 2016, has been collected and analyzed retrospectively.

Results: Out of 81 cases, the maximum number (69) of patients were female (85.18%) and 12 (14.81%) were male. Mean age of selected patients was 37.82 years (standard deviation [SD] = 12.753). Range for age was 17-72 years. Mean weight of the patients was 59.725 kg (SD = 10.659) in the range of 34-92 kg. Total percentage of both bile duct injury and bile leakage were 1.23%. The total conversion was in 5 (6.17%) cases, out of which 4.34% of female population and 16.66% of male population undergone conversion.

Conclusion: Even though laparoscopic cholecystectomy is commonly performed surgery and with time and experience its surgical outcome improving day by day, with little precaution its complications rate can be further reduced.

Key words: Acute cholecystitis, Cholelithiasis, Gallbladder surgery, Gallstone disease, Laparoscopic cholecystectomy

INTRODUCTION

Gallstone disease is a one among oldest and major surgical problem known to medical's fraternity. First time in history in 1882, a German surgeon Carl August Langerbach performed the traditional open cholecystectomy with an opinion, that rather than stones itself, it is the gallbladder which is the source of all ailments.¹ Laparoscopic cholecystectomy which revolutionized the treatment of gallstone was first performed by Prof Dr. Erich Mühe of Germany in 1985. He performed 94 such procedures before another surgeon, Phillipe Mouret of Lyon, France, reported his first laparoscopic cholecystectomy in 1987.²

Nowadays, undoubtedly laparoscopic cholecystectomy has become the gold standard treatment for gallstone disease. Because of its advantages of non-invasive approach, early recovery and minimal complication, it has widely been practiced worldwide even as a day care surgery.³ In 2006, Tokyo Guidelines now clearly recommended laparoscopic cholecystectomy as the first option for the treatment of acute cholecystitis.⁴

In spite of laparoscopic cholecystectomy is now being performed very commonly for a long time and with experience complications associated with this is also reducing in frequency but still a lot of patients require conversion to open as well as surgical complications are
happening on regular basis. Keeping in view of all this we need to keep learning from sharing our experiences to update our self for sake of patient’s care and safety.

This study is aimed at updating the surgical fraternity with an individual experience of a series of cases undergone laparoscopic cholecystectomy in term of their patient’s epidemiology, clinical presentation, different complications encountered at a different stage of patient care, etc.

**MATERIALS AND METHODS**

For this retrospective descriptive study, data from the record of all cases of laparoscopic cholecystectomies performed by the main author himself during the period from 1 November, 2011, to 30 April, 2016, has been collected. A total of 81 cases \((n = 81)\) who have undergone laparoscopic cholecystectomies found to be eligible for study in term of detail availability of case record. Cases that have been converted to open surgery has also been included for this study.

Apart from demographic and clinical profile, e.g., age, sex, weight, symptoms and its duration, comorbidity, history of jaundice, history of endoscopic retrograde cholangiopancreatography (ERCP), past history of surgery; total duration of surgery (from making first incision to taking last suture), all intra- and post-operative events, e.g., Anatomy around Calot’s triangle, intraabdominal adhesions, conversion to open and its reason, intra- and post-operative different complications, total number of days of hospital stay which was counted since the day of admission which is in our case 2 days before the day of surgery, follow-up period looked into and evaluated in detail.

**Surgical Techniques**

All cases were done as an elective case at Lady Hardinge Medical College and Smt. S.K. Hospital, New Delhi, India. For pre-operative preparation, all patients were made medically fit in term of any associated medical comorbidities, diabetes control, cessation of smoking, treatment of other associated ailments, etc. Operative techniques followed according to recommended guideline and adhered to standard protocols traditionally prescribed and based on different recommended trials. All cases were done under general anesthesia. Strict antiseptic and aseptic protocols have been followed.

The position of the patient is kept supine and after insertions of all trocars, we tilt the patient in head up \((15^\circ)\) anti-Trendelenburg position. Once patient got anaesthetized and cleaned and draped, with formal palpation of abdomen we start the process of surgery by creating the pneumoperitoneum. In almost every case, it has been achieved by closed technique using Veress needle at either infra or supraumbilical incision depending on the case. We take utmost care during blind placement of Veress needle and confirming its intraperitoneal position to prevent inadvertent damage of intraperitoneal viscera.

Once desired intraperitoneal pressure reached which has been already set up at the maximum level of 14-16 mm of Hg, first blind trocar of 10-11 mm at infra or supraumbilical location inserted. Through this port, we placed the 30° camera and inspect the peritoneal cavity thoroughly for any injury or other findings if any. Once everything found to be in the proper condition we put rest of the ports which is 10-11 mm epigastric just below the liver edge, 5 mm right clavicular in subcostal area (just above the gall bladder), and another 5 mm near right anterior axillary line on the line of the second working port. All these ports inserted under direct camera vision.

In next step, we clear any adhesions carefully using electrocautery if present there to visualize and free the gall bladder. Then, an assistant retracts the gallbladder cranially toward right shoulder holding the fundus of the gall bladder with ratched grasper. Very tense and distended gall bladder as in a case of mucocele or empyema required aspiration of its content before it can be held. To expose the Calot’s triangle, we pull the infundibulum inferior and lateral with atraumatic nonlocking grasper. Using a Maryland’s forceps and judicious use of electrocautery we identify and dissect the cystic duct and artery carefully. We always follow the critical view of safety technique and never try to see the common bile duct.\(^7,8\)

Once the cystic duct and cystic artery are identified and confirmed beyond doubt both are clipped and divided, two clips on proximal side and one clip on gall bladder side. It may not be always possible to clip cystic artery before cystic duct in such circumstances we clip and divide the cystic duct before to make further dissection easy and safe. Finally, we dissect and detach the gallbladder from its liver bed using either hook, scissors or spatula depending on situations. Then, hemostasis is secured and gallbladder is extracted most of the time through epigastric port. At the end, area around liver and its bed thoroughly washed with irrigation cannula using normal saline.

We put the drain usually of 14-16 F size only in difficult cases, when not sure about the hemostasis or if there is suspicion of injury. All trocars are removed under direct vision and simultaneously pneumoperitoneum is evacuated completely. Our indications for conversion to open surgery are unable to define the anatomy of Calor’s triangle, excess
uncontrolled bleeding, bile duct or other visceral injuries and discovery of malignancy.9-13

RESULTS

During the mentioned period of 4 years and 5 months, 81 cases of laparoscopic cholecystectomy found to be operated by the main author. Out of 81 cases, the maximum number (69) of patients were female (85.18%) and 12 (14.81%) were male. The mean age of selected patients was 37.82 years (standard deviation [SD] = 12.753). The range for age was 17-72 years. Mean weight of the patients was 59.725 kg (SD = 10.659) in the range of 34-92 kg.

The average duration of hospital stay for the patients was 4.632 days (SD = 2.94) in range of 2-19 days. Average follow-up periods were 04.85 months (SD = 02.556) in range of 1-12 months. All patients related epidemiological information depicted in Table 1.

Among symptoms, the most common symptoms were dyspepsia followed by pain abdomen of different frequency and nature as described in Table 2. Only two patients had got past history of jaundice, but none of them was related to hepatobiliary surgical or obstructive problem. 27 patients (33.33%) who had got past history of abdominal surgery, was all female and except one patient who underwent open appendectomy, rest were having either lower segment cesarian section or hysterectomy. Four patients have got a history of ERCP (three stenting and one diagnostic). All important related history and clinical features are listed in Table 2.

All the operative details including post-operative complications are listed in Table 3. Pertaining to special mention here is conversion to open. The total conversion was in five (6.17%) cases, out of which 4.34% of female population and 16.66% of male population undergone conversion. A major reason for conversion was severe adhesions leading to unidentified Calot’s anatomy. One patient converted because of common bile duct injury detected intra-operatively. Total percentage of both bile duct injury and bile leakage were 1.23%.

Out of five converted cases, 2 (40%) were having history of ERCP. All cases who had history of ERCP took longer operative time out of more adhesions in the area of Calot’s triangle. More than 3% undergone more than usual bleeding during surgery which was managed successfully with packing for few minutes. One patient with already previous history of recurrent sub-acute obstruction developed intestinal obstruction on second post-operative day which was managed conservatively only.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Range</th>
<th>Average/Mean</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (in years)</td>
<td>17-72</td>
<td>37.827</td>
<td>12.753</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>69 (85.18%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>12 (14.81%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weight (in kg)</td>
<td>34-92</td>
<td>59.725</td>
<td>10.659</td>
</tr>
<tr>
<td>Duration of symptoms (in months)</td>
<td>2-24</td>
<td>07.087</td>
<td>04.047</td>
</tr>
<tr>
<td>Duration of hospital stay (in days)</td>
<td>2-19</td>
<td>04.632</td>
<td>02.944</td>
</tr>
<tr>
<td>Follow-up period (in months)</td>
<td>1-12</td>
<td>04.85</td>
<td>02.556</td>
</tr>
<tr>
<td>SD: Standard deviation</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Signs and symptoms and important history</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>H/o: Pain abdomen</td>
<td>48.46</td>
</tr>
<tr>
<td>Mild upper abdomen</td>
<td>48.46</td>
</tr>
<tr>
<td>Recurrent ac. colicky</td>
<td>37.15</td>
</tr>
<tr>
<td>Severe ac. presentation</td>
<td>06.69</td>
</tr>
<tr>
<td>H/o: Dyspepsia</td>
<td>88.46</td>
</tr>
<tr>
<td>H/o: Vomiting</td>
<td>24.21</td>
</tr>
<tr>
<td>H/o: Jaundice</td>
<td>02.46</td>
</tr>
<tr>
<td>H/o: Tenderness</td>
<td>18.51</td>
</tr>
<tr>
<td>H/o: Multiple ac. attack</td>
<td>49.38</td>
</tr>
<tr>
<td>H/o: Pain radiating to back</td>
<td>02.46</td>
</tr>
<tr>
<td>Past H/o: Abdominal surgery</td>
<td>09.87</td>
</tr>
<tr>
<td>LSCS-8</td>
<td>14.81</td>
</tr>
<tr>
<td>Lap tube ligation-12</td>
<td>2.46</td>
</tr>
<tr>
<td>LSCS with tube ligation-2</td>
<td>4.93</td>
</tr>
<tr>
<td>Abdominal hysterectomy-4</td>
<td>1.23</td>
</tr>
<tr>
<td>Open appendicectomy-1</td>
<td>1.23</td>
</tr>
<tr>
<td>Past H/o: ERCP</td>
<td>4 (4.93)</td>
</tr>
<tr>
<td>Co-morbidities</td>
<td></td>
</tr>
<tr>
<td>Hypertension – 6</td>
<td>7.40</td>
</tr>
<tr>
<td>Hypertension with diabetes mellitus II – 1</td>
<td>1.23</td>
</tr>
<tr>
<td>Diabetes mellitus Type-II – 2</td>
<td>2.46</td>
</tr>
<tr>
<td>Hypothyroidism – 4</td>
<td>4.93</td>
</tr>
<tr>
<td>Jaundice –1</td>
<td>1.23</td>
</tr>
<tr>
<td>COPD – 1</td>
<td>1.23</td>
</tr>
</tbody>
</table>

LSCS: Lower segment cesarean section, ERCP: Endoscopic retrograde cholangiopancreatography, COPD: Chronic obstructive pulmonary disease

DISCUSSION

Since the inception of laparoscopic cholecystectomy and with the advancement of time till date, surgeons keep adding their experiences in term of surgical outcome which ultimately improving the result of surgery tremendously.

Here in this series, even though all surgeries have been performed by a single surgeon, it has been done for a longer span of time of more than 4 years and this way lot of inference can be drawn toward more precise way.

There is no surprise in getting a maximum proportion of female patient even in our series as this is the usual trend of gallstone disease.14 Again in this series mean age was just below the 38 years which shows usual trend of occurrence of gallstone disease in relatively younger age group. Weight
wise result is also not different. Major reason for a longer hospital stay of few patients was either conversion to open or complications like bile leakage and post-operative intestinal obstruction in one patient.

Dyspepsia was the most common presenting symptoms in our series followed by the mild upper abdominal and recurrent colicky pain. About little above the 6% of patients were having an acute presentation as an acute cholecystitis. This seems to be a higher percentage of occurrence of acute cholecystitis in gallstone diseased population in comparison to other studies which has got it in the range below three percent. As most of the data are from western literature, we need to further confirm it through collection of data of Indian patient with gallstone disease having acute cholecystitis.

All of the patients who have got history of prior abdominal surgery were operated for lower abdominal condition, and we did not find any difficulties in these patients during laparoscopic cholecystectomies. A study reported by Akyurek et al. in 2005 also found the same thing that lower abdominal surgeries do not make the laparoscopic cholecystectomy difficult neither it affects the duration of surgery.

About little less than 2% patients of our series had a history of ERCP in the past and in all of these patient surgeries were comparatively difficult, took longer time and half of this required conversion. Among many, recently published study in world journal of surgery also supported this result.

About little more than 6% of the patients needed conversion. A report recently published this year by Rashid et al. found 7% of conversion rate in their series. A very popular nationwide case series reported by Adamsen et al. found percentage of bile duct injury, 1.3% in acute cases and below <1% in routine cases, percentage of bile leakage was 2.1%. In our series, percentage of both

### Table 3: Operative details including complications

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Average/Range/%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Operative time (in min)</td>
<td>Mean 53.68 min, Range=25-110 min, SD=18.88</td>
</tr>
<tr>
<td>Conversion to open surgery</td>
<td>Mean 06.17%, (04.34% of total female operated), (16.66% of total male operated)</td>
</tr>
<tr>
<td>Intra-operative findings</td>
<td></td>
</tr>
<tr>
<td>Mucocele – 4</td>
<td>(4.93%)</td>
</tr>
<tr>
<td>Empyema – 3</td>
<td>(4.34%)</td>
</tr>
<tr>
<td>Contracted gallbladder – 2</td>
<td>(2.46%)</td>
</tr>
<tr>
<td>Intahepatic gallbladder – 2</td>
<td>(2.46%)</td>
</tr>
<tr>
<td>Severe adhesions – 6</td>
<td>(7.40%)</td>
</tr>
<tr>
<td>Sub hepatic drain</td>
<td>10 (12.34%)</td>
</tr>
<tr>
<td>Needed some local hemostatic substance (e.g., surgical)</td>
<td>4 (4.93%)</td>
</tr>
<tr>
<td>Complications:</td>
<td></td>
</tr>
<tr>
<td>1. Intraoperative</td>
<td></td>
</tr>
<tr>
<td>Bleeding (Total-3)</td>
<td></td>
</tr>
<tr>
<td>Gall bladder perforation</td>
<td>4 (4.93%)</td>
</tr>
<tr>
<td>Bile duct injury</td>
<td>1 (1.23%)</td>
</tr>
<tr>
<td>Bowel injury</td>
<td>0</td>
</tr>
<tr>
<td>Mortality</td>
<td>0</td>
</tr>
<tr>
<td>2. Post-operative</td>
<td></td>
</tr>
<tr>
<td>Severe and prolonged pain</td>
<td>6 (7.40%)</td>
</tr>
<tr>
<td>Bile leak</td>
<td>1 (1.23%)</td>
</tr>
<tr>
<td>Blood in drain (&gt;50 ml)</td>
<td>3 (4.34%)</td>
</tr>
<tr>
<td>Required blood transfusion</td>
<td>2 (2.46%)</td>
</tr>
<tr>
<td>Intestinal obstruction</td>
<td>1 (1.23%)</td>
</tr>
<tr>
<td>Port site infection</td>
<td>4 (4.93%)</td>
</tr>
<tr>
<td>Jaundice</td>
<td>0</td>
</tr>
<tr>
<td>Mortality</td>
<td>0</td>
</tr>
<tr>
<td>3. Follow-up</td>
<td></td>
</tr>
<tr>
<td>Required re-admission (Total-3)</td>
<td></td>
</tr>
<tr>
<td>2 for non-specific pain and abdominal distension</td>
<td>(2.46%)</td>
</tr>
<tr>
<td>1 was a case of bilioma</td>
<td>(1.23%)</td>
</tr>
</tbody>
</table>

SD: Standard deviation
bile duct injury and bile leakage were 1.23% which is acceptable. A patient who developed intestinal obstruction was already a known case with the recurrent history of sub-acute obstruction in the past and was not related to lap cholecystectomy surgery.

CONCLUSION

Laparoscopic cholecystectomy is very commonly performed and safe surgery now a day and with experience, its surgical outcomes are improving day by day. After learning from past experience and taking some precautionary measure as per recommendations and guidelines, complications rate can be reduced further.

REFERENCES

Effect of Pregabalin Premedication on the Laryngoscopic Response and Intra-operative Hemodynamic Variables in Laparoscopic Cholecystectomy: A Randomized Comparison of Two Doses

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Abstract

Background: Pre-operative medication has a vital role in anesthesia. Pregabalin is a newer drug of gabapentenoid class and is 6 times more potent than gabapentin. It has anxiolytic, sedative, antiallodynic, antihyperalgesic, antinociceptive, and antisecretory properties. This study was designed to know the effectivity of pregabalin as a premedication on the arterial pressor response to laryngoscopy and on hemodynamic variables.

Materials and Methods: This study was conducted on 90 patients of ASA Grade I and II of age group 20-60 years, undergoing laparoscopic cholecystectomy under general anesthesia. They were allocated to one of the three groups of 30 patients each. Group I received tablet diazepam 10 mg HS and 5 mg 1 h before surgery, Group II received capsule pregabalin 75 mg HS and 150 mg 1 h before surgery, and Group III received capsule pregabalin 75 mg HS and 300 mg 1 h before surgery. General anesthesia was induced and maintained by using standard technique. Level of sedation, heart rate, systolic, diastolic, and mean blood pressures (0, 1, 3, 5, 10, 15 min, and intraoperatively every 15 min) were recorded.

Results: Mean age, weight and sex distribution, and duration of laryngoscopy in all the three groups were comparable. Pregabalin 75 mg at night and 150 or 300 mg 1 h before surgery adequately attenuates pressor response to laryngoscopy and intubation. Patients' hemodynamic variables were more stable in pregabalin groups as compared to control group (diazepam) during the intra-operative period.

Conclusion: Oral pregabalin is more effective in blunting the cardiovascular response to laryngoscopy as compared to diazepam, when administered as premedication. Both pregabalin 150 mg and 300 mg were equally effective in diminishing the cardiovascular response to laryngoscopy and reducing the intra-operative hemodynamic perturbations.

Key words: Cardiovascular response to laryngoscopy, Intra-operative hemodynamic variables, Pregabalin

INTRODUCTION

An ideal premedication drug should relieve anxiety, produce amnesia and sedation, decrease secretions, prevent nausea and vomiting, and suppress hemodynamic response to laryngoscopy and intubation.¹ Traditionally, benzodiazepines such as midazolam and diazepam have been used. Gabapentinoids which include gabapentin and pregabalin are new class of drugs which binds to α2-δ protein subunit of voltage-gated calcium channels and inhibits the release of excitatory neurotransmitters in the central and peripheral nervous system.²

The objective of our study was to compare the effect of two doses of pregabalin and diazepam as a premedication agent, on the attenuation of cardiovascular response...
to laryngoscopy/intubation and on the intra-operative hemodynamic parameters in patients undergoing laparoscopic cholecystectomy under general anesthesia.

**MATERIALS AND METHODS**

After taking approval from the Institutional Ethics Committee and written informed consent from all patients, 90 ASA I/II patients aged 20-60 years, scheduled for laparoscopic cholecystectomy under general anesthesia, were randomly divided into three groups and were premedicated as per group allotted:

- **Group I:** Tablet diazepam 10 mg HS and 5 mg 1 h before surgery
- **Group II:** Capsule pregabalin 75 mg HS and 150 mg 1 h before surgery
- **Group III:** Capsule pregabalin 75 mg HS and 300 mg 1 h before surgery.

Randomization was done using random number table generated from computer software. Random drug/placebo assignment in the three groups was placed in serially numbered, opaque, sealed, identical envelopes by one of the senior anesthesiologists who was not involved with the study. For external uniformity of drugs, diazepam tablets were put inside empty capsules. The anesthesiologist administering drug/conducting anesthesia was blinded to the drug administered. Patients with impaired hepatic and renal function, cardiovascular disorders, on calcium channel blockers, antidepressants and oral hypoglycemic agents, drug allergy, and pregnant were excluded from the study.

General anesthesia was induced with fentanyl citrate (1 µg/kg), thiopentone sodium (till the abolition of eyelash reflex), and rocuronium bromide (1 mg/kg). Laryngoscopy and intubation were done after 90 s, and hemodynamic parameters were recorded. No surgical intervention was allowed till 15 min after intubation. N₂O (66%), O₂ (33%), sevoflurane (1%), and injection rocuronium (0.2 mg/kg) were used for the maintenance of anesthesia. An increase in pulse rate and blood pressure (BP) (>20%), lacrimation, and sweating in the presence of normal end-tidal carbon dioxide were treated with an additional dose of fentanyl (0.5 µg/kg). Response was checked after 10 min; nonresponders were managed by an incremental increase of sevoflurane till hemodynamic normalization. Patients were reversed and trachea was extubated at the end of the surgery.

Pre- and post-operative sedation was assessed in all the three groups using 5-point scale (Table 1). Heart rate (HR) and systolic BP (SBP), diastolic BP (DBP), and mean arterial pressure (MAP) were recorded before premedication, at induction, immediately (0 min) and 1, 3, 5, 10, and 15 min after laryngoscopy, at skin incision, start of pneumoperitoneum, and every 15 min thereafter till the completion of the surgery. Electrocardiogram, SpO₂, and EtCO₂ were also monitored continuously throughout the procedure.

Assuming a 5% dropout rate, the final sample size was set at 90 patients which would permit a Type I error of α to be 5%, with a Type II error of β to be 50%, and power of 80%. The results obtained were presented in a tabulated form, and statistical analysis was performed using the Statistical Package for Social Sciences software, Windows, version 14.0. Data were analyzed using Mann–Whitney, Chi-square, ANOVA, Kruskal–Wallis, and T-tests as appropriate. P < 0.05 was considered statistically significant and <0.001 as highly statistically significant. The failure rate of the drug was defined as >30% increase in hemodynamic parameters from the baseline values.

**RESULTS**

Demographic data, duration of laryngoscopy, and duration of surgery were comparable in all the three groups (Table 2). Although female patients dominated in all the three groups, sex distribution was comparable.

**Table 1: Five-point sedation scale**

<table>
<thead>
<tr>
<th>Score 1 (Barely arousable)</th>
<th>Asleep, needs shaking or shouting to arise</th>
</tr>
</thead>
<tbody>
<tr>
<td>Score 2 (Asleep)</td>
<td>Eyes closed, arousable with soft voice or light touch</td>
</tr>
<tr>
<td>Score 3 (Sleepy)</td>
<td>Eyes opened, less active, and responsive</td>
</tr>
<tr>
<td>Score 4</td>
<td>Awake</td>
</tr>
<tr>
<td>Score 5</td>
<td>Agitated</td>
</tr>
</tbody>
</table>

**Mean HR Comparison (T-test)**

Group I - as shown in Table 3, there was a mild increase in HR from a basal value of 87.67 ± 14.82 beats per minute (bpm) to 91.83 ± 15.07 bpm after premedication but before the induction of anesthesia. This was increased to a highly significant value of 114.07 ± 17.52 bpm at 0 min of intubation. After that, it came down to 113.47 ± 17.29 bpm at 1 min, 112.73 ± 17.46 bpm at 3 min, 107.30 ± 15.41 bpm at 5 min, 103.27 ± 14.39 bpm at 10 min, and 97.17 ± 13.40 bpm at 15 min post-intubation, which was still highly significant as compared to the baseline values.

Group II - there was a mild increase in HR from baseline value of 86.40 ± 12.71 bpm to 91.93 ± 18.46 bpm on OT table before the induction of anesthesia. Laryngoscopy resulted in an abrupt increase to 100.73 ± 18.65 bpm at 0 min. After that, it started falling, but remained highly
significant till 3 min of laryngoscopy and significant at 5 min (94.33 ± 15.46 bpm) of laryngoscopy. It came back to almost a basal value of 90.83 ± 15.86 bpm at 10 min and even lower to 85.97 ± 10.18 bpm at 15 min post-intubation.

Group III - on OT table, mean HR increased mildly from baseline value of 86.76 ± 13.74 bpm to 90.18 ± 15.55 bpm after premedication but before the induction of anesthesia. It further increased abruptly at 0 min of laryngoscopy to 103.84 ± 18.20 bpm. The values remain highly significant only up to 3 min (101.34 ± 17.70 bpm) of laryngoscopy. After that, it started falling and became statistically insignificant at 5 min. The values almost touched to baseline at 15 min post-intubation (89.03 ± 13.75 bpm).

This shows that a rise in HR following laryngoscopy and intubation was for a shorter duration in pregabalin groups (insignificant at 10 min in Group II and at 5 min in Group III) as compared to Group I, in which the rise was still highly significant at 15 min post-intubation.

As shown in Table 3, the basal HR values were comparable between the three groups (P ≥ 0.05). The difference in rise in HR following laryngoscopy and intubation at all time intervals (0-15 min) was highly significant between control and pregabalin groups. This difference was insignificant between Groups II and III.

**MAP Comparison (T-test)**

Group I - as shown in Table 4, there was statistically highly significant rise in MAP at 0, 1, and 5 min after intubation which though started falling, reached to baseline only after 15 min (90.60 ± 9.02 mm Hg) post-intubation.

Group II - there was a statistically insignificant and transient rise in MAP at 0 min after intubation which came below baseline at 1 min (89.23 ± 9.34 mm Hg). After that, there was a gradual but highly significant fall in MAP till 15 min post-intubation but did not require any treatment.

### Table 2: Patient characteristics

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Group I</th>
<th>Group II</th>
<th>Group III</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>34.97±11.95</td>
<td>35.50±9.46</td>
<td>36.97±8.22</td>
<td>0.73</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>53.47±12.32</td>
<td>53.83±9.79</td>
<td>58.33±10.91</td>
<td>0.17</td>
</tr>
<tr>
<td>Sex (F/M)</td>
<td>29/1</td>
<td>27/3</td>
<td>25/5</td>
<td>0.23</td>
</tr>
<tr>
<td>Duration of laryngoscopy (s)</td>
<td>10.10±1.73</td>
<td>10.40±1.59</td>
<td>10.30±1.68</td>
<td>0.46</td>
</tr>
<tr>
<td>Duration of surgery (min)</td>
<td>67.33±30.33</td>
<td>68.33±29.49</td>
<td>71.67±27.92</td>
<td>0.91</td>
</tr>
</tbody>
</table>

### Table 3: Changes in heart rate at different time intervals following laryngoscopy and intubation

<table>
<thead>
<tr>
<th>Time interval</th>
<th>Group I</th>
<th>Group II</th>
<th>Group III</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before pre-medicine</td>
<td>87.67±14.82</td>
<td>86.40±12.71</td>
<td>86.76±13.74</td>
<td>0.724</td>
</tr>
<tr>
<td>Before intravenous-induced</td>
<td>91.83±15.07</td>
<td>91.93±18.46</td>
<td>90.18±15.55</td>
<td>0.982</td>
</tr>
<tr>
<td>0 min</td>
<td>114.07±15.52 (P=0.000)</td>
<td>100.73±18.65 (P=0.000)</td>
<td>103.84±18.20 (P=0.000)</td>
<td>0.006</td>
</tr>
<tr>
<td>1 min</td>
<td>113.47±17.29 (P=0.000)</td>
<td>99.00±18.77 (P=0.000)</td>
<td>103.33±18.22 (P=0.000)</td>
<td>0.003</td>
</tr>
<tr>
<td>3 min</td>
<td>112.73±17.46 (P=0.000)</td>
<td>97.73±15.41 (P=0.000)</td>
<td>101.34±17.70 (P=0.000)</td>
<td>0.001</td>
</tr>
<tr>
<td>5 min</td>
<td>107.30±15.41 (P=0.000)</td>
<td>94.33±15.46 (P=0.017)</td>
<td>97.36±16.83 (P=0.017)</td>
<td>0.002</td>
</tr>
<tr>
<td>10 min</td>
<td>103.27±14.39 (P=0.000)</td>
<td>90.83±15.86 (P=0.182)</td>
<td>93.89±16.43 (P=0.613)</td>
<td>0.002</td>
</tr>
<tr>
<td>15 min</td>
<td>97.17±13.40 (P=0.000)</td>
<td>85.97±10.18 (P=0.864)</td>
<td>89.03±13.75 (P=0.340)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

### Table 4: Changes in mean blood pressure at different time intervals following laryngoscopy and intubation

<table>
<thead>
<tr>
<th>Time interval</th>
<th>Group I</th>
<th>Group II</th>
<th>Group III</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before pre-medicine</td>
<td>90.80±11.02</td>
<td>90.93±8.09</td>
<td>90.27±8.06</td>
<td>0.958</td>
</tr>
<tr>
<td>Before intravenous-induced</td>
<td>93.73±11.13 (P=0.080)</td>
<td>91.07±9.38 (P=0.926)</td>
<td>91.83±8.01 (P=0.247)</td>
<td>0.320</td>
</tr>
<tr>
<td>0 min</td>
<td>110.80±12.47 (P=0.000)</td>
<td>93.93±10.13 (P=0.086)</td>
<td>95.40±10.13 (P=0.920)</td>
<td>0.000</td>
</tr>
<tr>
<td>1 min</td>
<td>106.13±11.59 (P=0.000)</td>
<td>89.23±9.34 (P=0.323)</td>
<td>92.07±10.31 (P=0.373)</td>
<td>0.000</td>
</tr>
<tr>
<td>3 min</td>
<td>99.70±11.50 (P=0.001)</td>
<td>88.17±10.93 (P=0.124)</td>
<td>89.40±9.27 (P=0.699)</td>
<td>0.000</td>
</tr>
<tr>
<td>5 min</td>
<td>96.03±9.74 (P=0.036)</td>
<td>84.60±10.47 (P=0.001)</td>
<td>85.50±7.87 (P=0.007)</td>
<td>0.000</td>
</tr>
<tr>
<td>10 min</td>
<td>91.03±8.24 (P=0.925)</td>
<td>82.77±11.20 (P=0.000)</td>
<td>83.70±8.33 (P=0.001)</td>
<td>0.002</td>
</tr>
<tr>
<td>15 min</td>
<td>90.60±8.02 (P=0.937)</td>
<td>80.37±9.04 (P=0.000)</td>
<td>83.17±10.58 (P=0.004)</td>
<td>0.000</td>
</tr>
</tbody>
</table>

*P values in brackets show changes as compared to baseline (intragroup comparison).*
Group III - there was statistically non-significant and transient rise in MAP at 0 min (95.40 ± 10.13 mm of Hg) and 1 min (92.07 ± 10.31 mm of Hg) after intubation. After that, there was a gradual fall in MAP which was highly significant at 3, 5, 10, and 15 min of intubation. This fall did not require any treatment clinically and came back to normal after surgical stimulus.

The above findings show that a rise in MAP following laryngoscopy and intubation was highly significant at 0-5 min interval in Group I as compared to the baseline values. Whereas pregabalin groups (II and III) showed only an insignificant rise in MAP at 0 min of intubation.

As shown in Table 5, there was a highly significant difference in Group II and Group III as compared to Group I at all time intervals (0-15 min of intubation). On the other hand, there was no statistical difference in Group II compared to Group III. The fall in MAP afterward (3-15 min) was also highly significant statistically in Group II and Group III. Although this fall was statistically significant, it was clinically insignificant and did not require any active intervention.

This shows that both pregabalin 150 mg and 300 mg were equally effective and able to attenuate MAP completely as compared to control group.

Intra-operative Hemodynamic Stability Comparison (Paired t-test)

Group I - As shown in Table 5, there was a definite rise in all the hemodynamic parameters; average HR (diff = +13.89), SBP (diff = +14.04), DBP (diff = +16.05), and MAP (diff = +14.93) from the baseline values during intra-operative period. In addition, all these raised parameters were both statistically as well as clinically highly significant.

Group II - there was a fall in average HR (diff = −1.40) and SBP (diff = −4.98) during intra-operative period as compared to basal values. This fall was statistically significant in case of SBP and insignificant in case of HR. In addition, there was a mild rise in average DBP (diff = +2.01) and MAP (diff = +0.34) which was statistically as well as clinically non-significant.

Group III - intraproactively, there was a slight decrease in average SBP (diff = −0.36) as compared to baseline which is statistically insignificant. At the same time, there was a rise in average DBP (diff = +4.33), MAP (diff = +3.88), and HR (diff = +2.30) from baseline parameters. Variation in DBP and MAP was statistically significant, and in HR, it was insignificant. However, changes in all the parameters were clinically insignificant.

This shows that intra-operative hemodynamic parameters were more stable in patients who received pregabalin premedication as compared to those who received diazepam.

The above findings show that a rise in MAP following laryngoscopy and intubation was highly significant at 0-5 min interval in control group as compared to the baseline values. Whereas pregabalin groups (II and III) showed only an insignificant rise in MAP at 0 min of intubation.

Only 1 patient in Group II and 2 patients in Group III suffered dizziness, which was statistically insignificant.

**DISCUSSION**

Pregabalin is a new synthetic molecule and a structural derivative of the inhibitory neurotransmitter gamma-aminobutyric acid. It is a z2-δ ligand that has analgesic, anticonvulsant, anxiolytic, and sleep-modulating activities. Pregabalin binds potently to the z2-δ subunit of calcium channels, resulting in a reduction in the release of several neurotransmitters, including glutamate, noradrenaline, serotonin, dopamine, and substance P.

The present study was undertaken to evaluate the clinical efficacy of two different doses of pregabalin 150 mg and 300 mg as a premedicant.

**Table 5: Intraoperative hemodynamic stability in all the three groups**

<table>
<thead>
<tr>
<th>Group</th>
<th>SBP before pre-medicine</th>
<th>SBP average intra-operative</th>
<th>DBP before pre-medicine</th>
<th>DBP average intra-operative</th>
<th>MBP before pre-medicine</th>
<th>MBP average intra-operative</th>
<th>HR before pre-medicine</th>
<th>HR average intra-operative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group I</td>
<td>120.17±13.62</td>
<td>134.21±14.15</td>
<td>75.43±10.11</td>
<td>91.49±8.73</td>
<td>90.80±11.02</td>
<td>105.73±9.11</td>
<td>87.67±14.82</td>
<td>101.56±13.88</td>
</tr>
<tr>
<td>Difference</td>
<td>+14.04</td>
<td>+16.05</td>
<td>+14.93</td>
<td>0.000</td>
<td>0.000</td>
<td>0.000</td>
<td>0.000</td>
<td>0.002</td>
</tr>
<tr>
<td>P value</td>
<td>0.001</td>
<td>0.001</td>
<td>0.001</td>
<td>0.000</td>
<td>0.000</td>
<td>0.000</td>
<td>0.000</td>
<td>0.000</td>
</tr>
<tr>
<td>Group II</td>
<td>119.40±9.03</td>
<td>114.42±9.38</td>
<td>77.70±10.18</td>
<td>90.93±8.09</td>
<td>91.28±8.10</td>
<td>86.40±12.71</td>
<td>84.99±10.47</td>
<td></td>
</tr>
<tr>
<td>Difference</td>
<td>−4.98</td>
<td>+2.01</td>
<td>+0.34</td>
<td>+0.34</td>
<td>−1.40</td>
<td>0.611</td>
<td>0.611</td>
<td>0.611</td>
</tr>
<tr>
<td>P value</td>
<td>0.013</td>
<td>0.396</td>
<td>0.856</td>
<td>0.856</td>
<td>0.856</td>
<td>0.856</td>
<td>0.856</td>
<td>0.856</td>
</tr>
<tr>
<td>Group III</td>
<td>117.47±10.92</td>
<td>117.10±9.17</td>
<td>78.33±8.88</td>
<td>90.27±8.60</td>
<td>94.14±8.15</td>
<td>86.20±14.05</td>
<td>88.50±9.48</td>
<td></td>
</tr>
<tr>
<td>Difference</td>
<td>−0.36</td>
<td>+4.33</td>
<td>+3.88</td>
<td>+3.88</td>
<td>+2.30</td>
<td>+2.30</td>
<td></td>
<td></td>
</tr>
<tr>
<td>P value</td>
<td>0.877</td>
<td>0.025</td>
<td>0.047</td>
<td>0.047</td>
<td>0.392</td>
<td>0.392</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

MBP: Mean blood pressure, HR: Heart rate, SBP: Systolic blood pressure, DBP: Diastolic blood pressure
There were no significant differences between the three groups with respect to mean age, weight, and sex of patients. The duration of laryngoscopy and duration of surgery were comparable and statistically insignificant among all the three groups.

The rise in HR following laryngoscopy and intubation was highly significant in all the three groups at 0 min of intubation. However, this rise was of shorter duration in pregabalin groups as compared to control group, in which the rise in HR was still highly significant at 15 min of intubation. In addition, intergroup comparison shows that although rise in HR was not completely attenuated by pregabalin, it had a blunting effect on HR at all time intervals (0-15 min) after laryngoscopy and intubation as compared to control group.

As far as changes in BP are concerned, the changes in SBP followed the same pattern as the changes in diastolic BP. Hence, the changes in MAP are taken as the reflection of the effect of premedication on the attenuation of pressor response to laryngoscopy and intubation. There was a highly significant rise in MAP in diazepam group at 0 min of intubation, and this rise remains statistically highly significant till 5 min. After that, it became insignificant and touched baseline only at 15 min. Whereas in pregabalin groups, a very slight rise in MAP was observed at 0 min of intubation. This rise was statistically insignificant and transient. MAP values in both these groups touched the baseline at 1 min post-intubation and followed a decreasing trend after that till 15 min in the absence of surgical stimulus. This fall was statistically significant but clinically acceptable. Intergroup comparison shows that both the doses of pregabalin were equally effective and able to attenuate pressor response completely as compared to diazepam, in which rise was highly significant from 0 to 5 min.

Our findings are in concordance with Memis et al. and Kong and Irwin, who studied the effect of gabapentin on the attenuation of pressor response to laryngoscopy and intubation. A dose response study was conducted by Rastogi et al. to evaluate the clinically effective dose of oral pregabalin for the attenuation of pressor response to intubation by administering pregabalin 75 mg and 150 mg 1 h prior to induction. They reported that HR increased significantly immediately after laryngoscopy and intubation in all the groups, but it was least with 150 mg of pregabalin. This study also showed result similar to ours.

Memis et al., used gabapentin for the attenuation of cardiovascular response to laryngoscopy and intubation because of its synergistic action and analgesic properties, same as that of morphine. They found that oral administration of 800 mg gabapentin is effective in the attenuation of arterial BP and HR in 1, 3, and 5 min after laryngoscopy and endotracheal intubation. Proposed mechanism of pregabalin remains unknown. However, it is mainly due to the inhibition of calcium efflux from muscle cells with a consequent inhibition of smooth muscle relaxation, antinociceptive property, and a decrease in neuronal hyperexitability, as was hypothesized for gabapentin which might explain the effectiveness of pregabalin in the attenuation of hemodynamic response to laryngoscopy and intubation.

A similar observation was also noted by Eren et al. who studied the effect of pregabalin 150 mg on cardiovascular response to tracheal intubation in patients undergoing lumbar discal hernia repair. HR was significantly lower in the pregabalin group during and after intubation.

As shown in Table 5, the change in intra-operative HR and SBP, DBP, and mean BP were all in an increasing trend as compared to baseline in Group I whereas Group II/III showed either a statistically insignificant rise or a decrease in all the four parameters.

No other worker has reported the effect of pregabalin on intra-operative hemodynamic parameters. Our study shows that hemodynamic fluctuations were less in pregabalin group as compared to control group (diazepam) during the intraoperative period.

Side effects in the form of dizziness, lightheadedness, confusion, and ataxia are described with pregabalin in literature. However, in our study, only 1 patient in Group II and 2 patients in Group III suffered from dizziness which was statistically insignificant (Chi-square test).

**CONCLUSION**

In patients undergoing laparoscopic cholecystectomy under general anesthesia, oral pregabalin is more effective in blunting the cardiovascular response to laryngoscopy as compared to diazepam, when administered as premedication. Both pregabalin 150 mg and 300mg were equally effective in diminishing the cardiovascular response to laryngoscopy and reducing the intra-operative hemodynamic perturbations.

**REFERENCES**


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Role of Ultrasonography to Differentiate Benign and Malignant Thyroid Nodules in Correlation with Fine-needle Aspiration Cytology

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Abstract

Introduction: The thyroid gland is the largest of all endocrine glands and is the only one which is amenable to direct physical examination because of its superficial location. Superficial location of the thyroid gland allows excellent visualization and evaluation of its normal anatomy and pathologic condition by high resolution real-time gray-scale sonography.

Purpose: The objective was to use sonographic criteria to differentiate benign and malignant thyroid nodules and correlate with fine-needle aspiration cytology (FNAC) findings.

Materials and Methods: From June 2014 to August 2015, 70 cases of thyroid nodules based on inclusion and exclusion criteria were included in this study. The sonographic characteristics of each nodule were determined. The results were then compared with FNAC/histopathological diagnosis.

Results: Of the 70 nodules examined, 6 (8.57%) were found to be malignant on cytopathology. The malignant nodules demonstrated solid or predominantly solid composition (sensitivity 100% and specificity 9.37%); presence of microcalcification (sensitivity 66.6% and specificity 98.4%); irregular or poorly defined margins (sensitivity 83.3% and specificity 92.06%); anteroposterior diameter more than transverse diameter (sensitivity 50% and specificity 93.75%); absent or thick incomplete halo (sensitivity 83.3% and specificity 82.8%); markedly hypoechoic character (sensitivity 66.6% and specificity 90.6%).

Conclusion: Gray-scale ultrasonography (USG) features of thyroid nodules are useful to distinguish benign and malignant thyroid nodules. From our study, it is apparent that the USG findings of poorly defined margins, marked hypoechoicinity, microcalcifications, absent or thick irregular peripheral halo, and a taller-than-wider shape have a high diagnostic accuracy for identifying malignant thyroid nodules.

Key words: Fine-needle aspiration cytology, Follicular adenoma, Hyperplastic nodule, Papillary carcinoma, Thyroid nodule, Ultrasound

INTRODUCTION

Nodular thyroid disease is detected in 3-7% of the adult population worldwide. They are common in females with a ratio of 5:1 and prevalence mainly depend on age, sex, iodine intake, diet (goitrogen) therapeutic, and environmental exposure. The majority of these cases are clinically occult but readily detected by high-resolution ultrasonography (USG).1-4

Thyroid cancer is rare and accounts for <1% of all malignant neoplasms. It has a good long-term prognosis after surgical excision. The high prevalence of thyroid nodules in the general population calls for a clear strategy to identify patients in whom surgical excision is genuinely indicated as opposed to those who can be managed conservatively.3 Current management guidelines state that diagnostic USG should be performed in all patients with thyroid nodules and fine-needle aspiration cytology (FNAC) in nodules more than 1.5 cm or which are potentially malignant or...
indeterminate on USG. Basic use of sonography in nodular thyroid is to determine the location of palpable neck mass, characterize nodule as benign or malignant, know about extent of thyroid malignancy, and guide fine-needle aspiration of the thyroid nodule or cervical lymph node.

The categorization of thyroid nodules into benign and malignant nodules by USG is very important as it helps in the further management of the patients with nodular thyroid disease. Hence, to find out the efficacy of USG in the evaluation of thyroid nodules, the present study is undertaken.

MATERIALS AND METHODS

Based on the inclusion and exclusion criteria, 70 cases of thyroid nodules, diagnosed by ultrasound were included in this study between June 2014 and August 2015. The ultrasound examination was done in the Department of Radiology, MGM Hospital, Warangal, using high-frequency linear array ultrasound transducer. These cases were subjected to FNAC for confirmation of ultrasound findings and establishment of diagnosis. The nodules, which were diagnosed on FNAC as follicular neoplasms, were operated, and biopsy was sent for histopathological examination to differentiating follicular adenoma and follicular carcinoma.

Inclusion Criteria

- All the patients with thyroid nodule detected on ultrasound which is more than 1.5 cm in size were included in the study.
- All patients with thyroid nodules suspicious of malignancy, irrespective of its size.

Exclusion Criteria

- All patients with diffuse thyroid enlargement.

Equipment

In the present study, gray-scale real-time ultrasound examination was done using 7.5 MHz linear array transducer. Ultrasound machines used were Esaote Mylab Classic and Esaote Mylab 40.

Technique of Examination

The patient is examined in the supine position with an extended neck. A pillow is placed under the shoulders to provide better exposure of the neck. Since the gland is situated superficially, 7.5 MHz linear array transducer is used.

The entire thyroid gland from upper to the lower pole and the isthmus is examined in the longitudinal and transverse planes. Bilateral carotid arteries, jugular veins, and supraclavicular fossa are also examined.

FNAC Technique

Before the ultrasound-guided FNAC, the neck is hyperextended, and the skin is cleansed with povidone-iodine (Betadine) solution. The transducer is also cleansed with the same solution. Sterile gel is used as a coupling agent. In the present study, we used 7.5 MHz linear transducer to take FNAC. Then, the needle is held in one hand and the transducer in the other. The needle is inserted through the skin of thyroid region in front of the neck at an oblique angle within the image plane of the transducer.

The needle used for thyroid FNAC is standard 25-gauge, non-cutting beveled edge needle. The needle is attached to 10 ml syringe. After introducing the needle, the needle is moved gently up to the nodule center under the US guidance. Then, gentle suction is done by putting the piston of the syringe. If the specimen contains much blood, a non-aspiration technique is used. In this, 25-gauge needle is inserted under ultrasound guidance into the thyroid gland and no suction is applied, and this needle is moved in back and forth excursions. Due to capillary action, the fluid of cells from the nodule move the needle such fluid specimen is often less bloody. Two drops of the aspirate/fluid in the syringe are ejected over a clean slide and with the help of the other blank slide with 60° angle; the aspirate on the first slide is spread on it to form a film of coating on it. The slide making procedure is repeated once more and after smearing the second slide, these slides are put in a jar containing absolute alcohol for fixation. These two slides in alcohol along with container are sent to the pathology department for cytopathological study.

OBSERVATIONS AND RESULTS

Of the 70 nodules evaluated at USG, 11 were diagnosed to be malignant, using five sonographic features such as shape of the nodule (taller than wide), marked hypoechogenicity, microcalcifications, poorly defined margins, absent or irregular thickened discontinuous peripheral halo (the presence of any two features in a thyroid nodule was considered malignant), and the rest of the nodules (59) were diagnosed as benign. After cytological/histopathological evaluation, 6 (8.57%) of the 70 nodules were found to be malignant and 59 (91.43%) were benign. 5 nodules, which were given as follicular neoplasms on FNAC, were diagnosed as follicular adenomas at histopathology. All the malignant nodules on FNAC were found to be papillary carcinomas.

The sonographic criteria used in the study were based on previously published criteria. The ultrasound diagnosis was compared with the pathological diagnosis and the sensitivity, specificity, positive predictive value, negative
predictive value, and diagnostic accuracy of ultrasound and five sonographic features (shape of the nodule [taller than wide], marked hypoechogenicity, microcalcifications, poorly defined margins, and absent or irregular thickened discontinuous peripheral halo) in predicting malignancy in a thyroid nodule were calculated using the statistical formulas. The \( P \) values were calculated for each of the sonographic feature using Chi-square test, and \( P \) value was found to be statistically significant (\( P < 0.0001 \)).

In this study, the youngest patient was 16 years of age and oldest 70 years. The maximum number of cases are seen in the age group of 31-40 years (41\%) and 41-50 years (25.7\%) with females (81.42\%) predominating over males (18.57\%) (Table 1).

The majority of the malignant nodules are ill defined with shape taller than wide. Microcalcifications are seen exclusively in malignant nodules. All the malignant nodules are profoundly hypoechogenic with the absence of well-defined peripheral halo. All malignant nodules are predominantly solid. However, the most of the solid nodules are benign.

Most of the benign nodules are well defined with thin peripheral continuous halo. All the nodules with peripheral eggshell calcifications are benign. The most of the benign nodules are predominantly solid; however, all the cystic lesions are benign. Shape of the benign nodule is oval with long axis along the transverse plane. All hyperechoic, isoechoic, and majority of hypoechoic nodules are benign (Table 2).

Microcalcifications have the highest accuracy in diagnosing malignant thyroid nodule followed by taller-than-wide shape, ill-defined margins, marked hypoechogenicity, and absent peripheral halo. The predominant solid character of malignant nodule on USG is not statistically significant and has a poor accuracy in diagnosing malignant thyroid nodules (Table 3).

Ultrasound correctly diagnosed malignancy in 5 out of 6 cases and falsely diagnosed 6 out of 64 benign nodules as malignant. The sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of ultrasound in predicting malignancy were found to be 83.33\%, 90.62\%, 45.45\%, 98.30\%, and 90\%, respectively (Table 4).

**DISCUSSION**

A thyroid nodule is defined as a discrete lesion within the thyroid gland that is distinguishable from the adjacent parenchyma at USG. In the present study, a maximum number of cases of thyroid nodules are seen in the age groups of 31-40 years (41\%) and 41-50 years (25.7\%) with females (81.5\%) predominating over males (18.5\%). The percentage of benign thyroid nodules (91.43\%) is higher than the malignant (8.57\%) thyroid nodules. These findings correlate with the previous similar studies, but the studies conducted by Popli et al. (18.33\%\(^{10}\)) and Lee et al. (37.69\%\(^{11}\)) showed the relatively increased proportion of malignant thyroid nodules compared to the present study.

The shape of the nodule has been studied as a marker of malignancy. The most of the malignant nodules in the present study showed shape that is taller than wide. In this study, the sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of the shape of the nodule being taller than wide in predicting malignancy is 50\%, 93.75\%, 42.85\%, 95.23\%, and 90\%, respectively. These findings confirm that shape of the nodule has a poor positive predictive value. However, its high specificity, negative predictive value, and accuracy make it a reliable feature in ruling out malignancy in a thyroid nodule on USG. The similar studies conducted

### Table 1: Age and sex wise distribution of thyroid nodules

<table>
<thead>
<tr>
<th>Age in years</th>
<th>Male</th>
<th>Female</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>11-20</td>
<td>0 (0.0)</td>
<td>3 (4.3)</td>
<td>3 (4.3)</td>
</tr>
<tr>
<td>21-30</td>
<td>1 (1.4)</td>
<td>12</td>
<td>13 (18.6)</td>
</tr>
<tr>
<td>31-40</td>
<td>4 (5.7)</td>
<td>25 (30.0)</td>
<td>29 (41.4)</td>
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<tr>
<td>41-50</td>
<td>5 (7.1)</td>
<td>13 (18.5)</td>
<td>18 (25.7)</td>
</tr>
<tr>
<td>51-60</td>
<td>2 (2.9)</td>
<td>4 (5.7)</td>
<td>6 (8.6)</td>
</tr>
<tr>
<td>61-70</td>
<td>1 (1.4)</td>
<td>0 (0.0)</td>
<td>1 (1.4)</td>
</tr>
<tr>
<td>Total</td>
<td>13</td>
<td>57</td>
<td>70 (100)</td>
</tr>
</tbody>
</table>

### Table 2: Distribution of ultrasound characteristics in benign and malignant thyroid nodules

<table>
<thead>
<tr>
<th>USG character</th>
<th>Malignant</th>
<th>Benign</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Margin</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Well-defined</td>
<td>2</td>
<td>59</td>
<td>61</td>
</tr>
<tr>
<td>Poorly defined</td>
<td>4</td>
<td>5</td>
<td>9</td>
</tr>
<tr>
<td>Calcification</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Present</td>
<td>4 (microcalcification)</td>
<td>10</td>
<td>14</td>
</tr>
<tr>
<td>Absent</td>
<td>2</td>
<td>54</td>
<td>56</td>
</tr>
<tr>
<td>Peripheral halo</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thin and continuous</td>
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<td>60</td>
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<tr>
<td>Absent or thick and regular</td>
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<td>5</td>
<td>10</td>
</tr>
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<td>Internal contents</td>
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<td></td>
<td></td>
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<tr>
<td>Solid/predominantly solid</td>
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<td>48</td>
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<td>Predominantly cystic</td>
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<td>3</td>
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<tr>
<td>Purely cystic</td>
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<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Echogenicity</td>
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<td>23</td>
</tr>
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<td>26</td>
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<tr>
<td>Hypoechoic</td>
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<td>11</td>
</tr>
<tr>
<td>Markedly hypoechoic</td>
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<td>0</td>
<td>4</td>
</tr>
<tr>
<td>Shape</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Taller than wide</td>
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<td>4</td>
<td>7</td>
</tr>
<tr>
<td>Not taller than wide</td>
<td>3</td>
<td>60</td>
<td>63</td>
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</tbody>
</table>

in the past show that shape of the nodule has statistically heterogeneous significance in predicting malignancy in thyroid nodules, though the study conducted by Lee et al. show 100% specificity and positive predictive value, which is significantly different from other studies.10-14

A nodule is considered markedly hypoechoic when it is relatively decreased in echotexture compared to the adjacent strap muscles of the neck. The previous similar studies have revealed that most malignancies demonstrate a hypoechoic nodule, yet most hypoechoic nodules are benign in view of the high prevalence of benign lesions.10-14 The most of the nodules in the present study are hyperechoic followed by isoechoic and hypoechoic. Only a few nodules were found to be markedly hypoechoic and are exclusively found in malignant thyroid nodules (4 out of 6; 66.66%). This indicates that presence of marked hypoechogenicity is a good predictor of malignancy in thyroid nodule on USG. The present study shows sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of marked hypoechogenicity in predicting malignancy of thyroid nodule is 83.33%, 92.06%, 45.45%, 98.30%, and 90 respectively.

Microcalcifications (Figures 1-3) are seen sonographically as multiple punctate bright echoes that are <2 mm in size, with or without acoustic shadowing.15 The current study showed that microcalcifications were exclusively seen in malignant nodules though not present in all cases of malignant thyroid nodules (not seen in 2 out of 6 cases). In the present study, microcalcifications were found to have the highest diagnostic accuracy (95.71%), specificity (98.46%), and negative predictive value (96.2%) compared to other sonographic characteristics on USG. Hence, it can be used as a reliable criterion in differentiating benign and malignant thyroid nodules on USG. The most of the previous studies show similar statistical significance, but the studies done by Remonti et al.14 and Lee et al.11 show relatively low sensitivity and accuracy.

When more than 50% of the margin of a thyroid nodule is not clearly defined, it is considered as poorly defined.16,17 Malignant lesions tend to have poorly defined or irregular spiculated margins. The previously reported sensitivity of poorly defined margins for diagnosing malignant nodules ranges widely from 8.3% to 77.5%.16,18 In this study, sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of poorly defined margins for diagnosing malignant nodules was found to be 83.33%, 92.06%, 45.45%, 98.30%, and 90% respectively, which was
Avinash, et al.: USG to Differentiate Benign from Malignant Thyroid Nodules

in malignant nodules with sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of 83.33%, 82.82%, 31.25%, 98.14%, and 82.85%, respectively. In a study conducted by Samghabadi et al., the absence of a halo was most predictive of malignancy on conventional USG. The sonographic feature of absent or irregular thick discontinuous peripheral halo has a relatively high specificity and negative predictive value making it a reliable feature to rule out malignancy on USG.

In the present study, compared to other sonographic features such as microcalcifications, poorly defined margins and marked hypoechogeticity, the shape of the nodule has a relatively low accuracy in predicting malignancy. However, the high negative predictive value makes it a good sonographic feature in ruling out malignancy.

The efficacy of USG in picking up malignancy in thyroid nodules was evaluated by comparing with pathological findings of the thyroid nodule. USG features of poorly defined margins, marked hypoechogeticity, and taller-than-wide shape were found to have high diagnostic accuracy for identifying malignant thyroid nodules. The present study showed that combination of sonographic features suggesting malignancy was more accuracy than a single sonographic feature as the study is based on the assumption that at least two features suggestive of malignancy should be present to diagnose a thyroid nodule as malignant.

The findings in other studies quoted in Table 5 correlate approximately with the present study, specially the study conducted by Popli et al. The study conducted by Kim et al. shows poor specificity, positive predictive value and accuracy of USG compared to other studies; the difference can be explained by the fact that they considered presence of even one sonographic criterion suggestive of malignancy is categorized as malignant nodule. This assumption will cause decrease in specificity and accuracy as relatively more false positives are diagnosed on USG in their study.

Of all the studies mentioned in Table 5, the study conducted by Lee et al. shows the highest specificity and negative predictive value with accuracy same as the present study. This study is based on the assumption that presence of any two of the above-mentioned features in a thyroid nodule was considered malignant, and the rest of the nodules were categorized as benign nodules which exactly mimics the present study (Table 5).
The Efficacy of USG in Predicting Benign Thyroid Nodules

The majority (64 out of 70; 91.42%) of the nodules in the present study were found to be benign, of which adenomatous nodule/colloid nodule/hyperplastic nodule is the most common type followed by follicular adenoma. In the present study, most benign nodules are well defined (92.18%) with regular, well-defined thin peripheral halo (92.14%), and growth is along the tissue planes, i.e. wider than tall in shape (93.75%). Calcifications are generally absent in benign nodules and even if seen, are usually macrocalcifications (peripheral eggshell calcification in 15.62% of benign nodules). The most of the benign nodules are usually solid (75%) with variable echogenicity. However, all cystic or predominantly cystic lesions are exclusively benign. Benign nodules can be hyperechoic (35.93%), isoechoic (40.62%), or hypoechoic (14.06%), but all hyperechoic and isoechoic nodules are benign. In summary, well-defined margins, well-defined thin peripheral halo, and wider than tall shape are commonly seen in benign nodules and are good predictors of benign nature of a nodule. Although calcification is not seen in benign nodules, the presence of macrocalcifications or peripheral eggshell calcifications (Figure 4) favors benign nature. Microcalcifications almost never occur in benign nodules. Although their echogenicity may vary, hyperechogenicity is exclusively noted in benign nodules.

The similar studies done in the past show that the sonographic criteria for predicting benign nature of a thyroid nodule are well-defined margins, well-defined thin peripheral halo, and wider than tall in shape and absence of calcifications (microcalcifications) though macrocalcifications can be seen.\textsuperscript{10,11}

CONCLUSION

Thyroid nodules commonly occur in females with mean age of incidence 39.5 years. Relative incidence of malignancy in thyroid nodules is higher in males compared to females. Overall incidence of malignant nodules is <10% with all the malignant nodules diagnosed as papillary carcinoma. The most of the thyroid nodules are benign (64 out of 70) with the most common type being hyperplastic thyroid nodule (59 out of 64). The US features such as marked hypoechogenicity, poorly defined margins, absent or thick irregular halo, microcalcifications, and a taller-than-wide shape were found to be good predictors of malignancy. Out of all the features mentioned above, microcalcifications are found to have the highest accuracy in predicting malignancy. The most of the malignant nodules are hypoechoic; however, predominant number of hypoechoic nodules are benign. The majority of benign

<table>
<thead>
<tr>
<th>Studies</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>PPV (%)</th>
<th>NPV (%)</th>
<th>Accuracy (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Present study</td>
<td>83.33</td>
<td>90.62</td>
<td>45.45</td>
<td>98.30</td>
<td>90</td>
</tr>
<tr>
<td>Popli et al.\textsuperscript{10}</td>
<td>81.81</td>
<td>87.24</td>
<td>59.01</td>
<td>95.53</td>
<td>86.25</td>
</tr>
<tr>
<td>Kim et al.\textsuperscript{12}</td>
<td>93.8</td>
<td>66</td>
<td>56.1</td>
<td>95.9</td>
<td>74.8</td>
</tr>
<tr>
<td>Lee et al.\textsuperscript{11}</td>
<td>72</td>
<td>100</td>
<td>100</td>
<td>86</td>
<td>90</td>
</tr>
<tr>
<td>Nilakantan et al.\textsuperscript{21}</td>
<td>20</td>
<td>97.67</td>
<td>Not available</td>
<td>Not available</td>
<td>Not available</td>
</tr>
</tbody>
</table>

USG: Ultrasonography, PPV: Positive predictive value, NPV: Negative predictive value
nodules are well defined with thin peripheral halo. The shape is wider than tall, and calcifications are rarely seen. All hyperechoic and cystic/predominantly cystic nodules are benign (Figures 5 and 6).

REFERENCES


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Impact of Antenatal Anxiety and Depression

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Abstract

Introduction: Pregnancy is generally accepted to be a time of happiness and emotional well-being for a woman. However, for many women, pregnancy increases their vulnerability to psychiatric illnesses such as depression and anxiety disorders (ANYAXs), and these are usually overlooked. This study was conducted to determine the effect of maternal depression and ANYAXs on the course of pregnancy and on fetal health.

Materials and Methods: A total of 310 women attending the antenatal clinic were interviewed as a part of this cohort study, of which 284 completed the study. The participants were assessed twice in the second trimester and once in the third trimester. Depressive and ANYAXs were diagnosed using ICD-10 criteria. Severity was assessed using relevant scales.

Result: The prevalence of depressive disorders was 41 (63%) and ANYAXs 24 ((36.9%). There was a significant association between the presence of psychiatric disorders (PSYDS) and obstetric complications ($P < 0.05$) and between depression in pregnancy and the development of hypertensive disorder of pregnancy ($P < 0.05$). ANYAX in pregnancy was significantly associated with fetal growth disorder ($P < 0.05$). The presence of a PSYDS was strongly associated with fetal distress measured by the Apgar score at birth ($P < 0.05$) and with preterm birth ($P < 0.05$).

Conclusion: An interdisciplinary approach is needed for improving interventions to prevent maternal and fetal complications.

Key words: Antenatal, Anxiety, Depression, Fetal growth, Pregnancy

INTRODUCTION

Pregnancy and its associated complications have been an issue of public health concern throughout the world. Pregnancy and the transition to parenthood involve major psychological and social changes in the mother, which have been linked to symptoms of anxiety and depression.¹ Approximately, 21% of women experience a mood disorder and 30% anxiety disorder (ANYAX) at some points in their lives.² Although historically it was believed that pregnant women are at lower risk of anxiety and mood disorders,³ recent studies do not support this belief. Rather between 10% and 27% of women experience depressive symptoms during pregnancy including 2-11% who experience major depressive disorder.

Studies have indicated that depression and anxiety during pregnancy affect the neonatal outcome. In particular, attention has focused on the increased risks of spontaneous preterm delivery, low birth weight, operative delivery (cesarean section and instrumental vaginal delivery), and admission to a neonatal intensive care unit among offspring of women with antenatal depression.⁴-⁶ Not only does depression tend to shorten pregnancy but also major life events, if they are perceived as stressful, tend to shorten it as well.⁷,⁸ Antenatal stress has been suggested to cause preterm delivery through activation of the placental-maternal pituitary-adrenal axis.⁹ This hypothesis is further supported by a relation between preterm birth and elevated levels of corticotropin-releasing hormone (CRH) in maternal plasma and in placenta.¹⁰,¹¹

Studies have shown a relationship between maternal anxiety in pregnancy and increased uterine artery resistance index.¹² It suggests a mechanism by which the psychological state of the mother may affect fetal development, and may explain epidemiological associations between maternal anxiety and low birth weight. High levels of anxiety during pregnancy have been associated with increased risk for preeclampsia.¹²

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The correlation between plasma levels of cortisol in the mother and in the fetus may have implications for the developing fetal brain.13

Depression during pregnancy has extensive negative effects on mothers and babies including increased risks for preterm birth and low birth weight.14,15 Posttraumatic stress disorder during pregnancy was shown to increase the risk for preterm birth.16

This study was conducted to determine the effect of maternal depression and ANYAXs on the course of pregnancy and on fetal health.

MATERIALS AND METHODS

This cohort study was carried out in the outpatient Department of Obstetrics and Gynecology at Goa Medical College, Bambolim - Goa, over a period of 1 year. Ethical approval was obtained from the Local Ethics Committee before commencing the study.

A total of 310 antenatal women were interviewed during this period. All the women were in the second trimester at the time of interview. This was essential because most women presented for the first antenatal visit during the second trimester or toward the end of the first trimester. Furthermore, the time period required to obtain the reports of routine investigations before induction in the study resulted in all women being inducted in the second trimester.

Informed consent was obtained from all patients before inclusion. Only those women who intended to carry out future antenatal visits and delivery at Goa Medical College were included in the study.

Antenatal visits in Goa Medical College (GMC) are carried out at intervals of 4 weeks up to 28 weeks, at intervals of 2 weeks up to 36 weeks, and weekly thereafter till term. Participants were assessed on 3 occasions; twice in the second trimester and once in the third trimester. Hence, antenatal assessments in the study were separated by a gap of at least 4 weeks.

Potential confounding factors or effect modifiers identified were age, parity, current substance use, caloric intake, obstetrical complications (OBSDYSs) in previous pregnancy which are likely to recur in subsequent pregnancies, any abnormality detected on routine investigation or booking ultrasound scan, medical and surgical illness during pregnancy, gynecological disorders in pregnancy, and if the patient was currently receiving medication for any psychiatric disorder (PSYDS).

After limiting the confounding factors and effect modifiers, participants were inducted in the study.

Inclusion criteria were:
1. Maternal age between 20 and 35 years
2. No history of substance use
3. No history of recurrent obstetric complications
4. Adequate caloric intake
5. Not receiving treatment for a major PSYDS currently
6. No abnormality detected on initial routine antenatal screening or on initial ultrasound.

Depressive and ANYAXs were diagnosed using the ICD-10 criteria.

Patients thus diagnosed were then rated to analyze the longitudinal course of the illness using relevant scales.

Data (psychiatric and medical) were recorded, coded, analyzed, and interpreted using the SPSS software.

RESULTS

A total of 310 antenatal women participated in the study. Of these, 12 women did not follow-up for further antenatal visits at GMC; 5 patients underwent a therapeutic abortion for severe complications in the second trimester, a further 5 patients developed PSYDSs following an adverse obstetric event (depression - 3 and panic disorder - 2) and 4 patients were started on medications during pregnancy for psychiatric symptoms (mania = 1, depression = 2, and generalized ANYAX = 1).

The number of participants who completed the study was 284 (attrition rate = 8.39%).

Findings in the study are described below.

Of the 284 patients who participated in the study, 65 (22.89%) were diagnosed as having a PSYDS.

The mean age of the patients who had a PSYDS was 23.88 (standard deviation 2.713) and the mean age of those who did not was 23.20 (standard deviation 2.415) as shown in Table 1.

Of the total of 65 patients who were diagnosed as having a PSYDS, 41 (63%) patients were diagnosed to have depressive disorders and 24 (36.9%) ANYAXs. The overall distribution of the various depressive and ANYAXs is summarized in Table 2.

Of the total of 65 patients who were diagnosed as having a PSYDS, 24, i.e., (36.9%) developed OBSDYSs.
Of the remaining 219 patients who did not have any psychiatric diagnosis, 44 (20.1%) developed OBSDYS as is shown in Table 3.

A significant association was found between the presence of PSYDSs and OBSDYSs (Chi-square = 8.381, P = 0.004).

Out of 41 patients with depression, 11 (26.8%) patients were diagnosed to have hypertension as compared to 31 (12.8%) patients out of 243 without depression.

Depressive disorders were significantly associated with the development of hypertensive disorder in pregnancy (Chi-square = 5.513, P = 0.019) as shown in Table 4.

Of the 24 (36.9%) patients diagnosed to have ANYAXs, 10 (41.7%) had fetal growth disorder (FGD) as compared to 43 (16.5%) patients with no ANYAX as shown in Table 5.

A significant association was found between the presence of ANYAXs in pregnancy and FGDs (Chi-square = 13.451, P < 0.05).

Of the 65 patients with anxiety and depressive disorders, 27 (41.5%) had abnormal Apgar score as compared to 51 (23.3%) with no PSYDS.

The presence of a PSYDS was strongly associated with fetal distress as measured by the Apgar score at birth as shown in Table 6 (Chi-square = 8.381, P = 0.04).

16 (24.6%) patients of those with PSYDS had preterm delivery as compared to 26 (11.9%) without PSYDS.

PSYDS in pregnancy was significantly associated with preterm birth as shown in Table 7 (Chi-square = 6.459, P < 0.01).

### DISCUSSION

The study was undertaken to determine the effect of anxiety and depression in the antenatal period and on the course of pregnancy and fetal health.

65 patients met the diagnosis of anxiety and depression. Of these, 63% were diagnosed to have depressive disorder and 36% ANYAXs. This is in sharp contrast with the study by Andersson et al., wherein the point prevalence of mood and ANYAXs during the second trimester of pregnancy in a population-based sample of pregnant women were analyzed using the Primary Care Evaluation of Mental Disorders questionnaire was found to be 10.2% for depression and 6.6% for ANYAXs. Studies anxiety

**Table 1: Mean age and standard deviation of participants**

<table>
<thead>
<tr>
<th>Psychiatric dysfunction</th>
<th>Number</th>
<th>Mean age</th>
<th>Standard deviation</th>
</tr>
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<tbody>
<tr>
<td>Present</td>
<td>65</td>
<td>23.88</td>
<td>2.713</td>
</tr>
<tr>
<td>Absent</td>
<td>219</td>
<td>23.20</td>
<td>2.415</td>
</tr>
</tbody>
</table>

**Table 2: Distribution of patients with depressive and ANYAXs**

<table>
<thead>
<tr>
<th>PSYDS</th>
<th>Number of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Depressive disorder</td>
<td>41 (63%)</td>
</tr>
<tr>
<td>Recurrent depressive disorder</td>
<td>18</td>
</tr>
<tr>
<td>Depressive episode</td>
<td>8</td>
</tr>
<tr>
<td>Generalized ANYAX</td>
<td>9</td>
</tr>
<tr>
<td>Depressive episode and panic disorder</td>
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</tr>
<tr>
<td>Depressive episode and obsessive compulsive disorder</td>
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</tr>
<tr>
<td>ANYAXs</td>
<td>24 (36.9%)</td>
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<td>Generalized ANYAX</td>
<td>12</td>
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<td>Obsessive-compulsive disorder</td>
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<td>Panic disorder</td>
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<td>Social phobia</td>
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**Table 3: Association between PSYDSs and obstetric dysfunction**

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<tr>
<td>Present</td>
<td>24</td>
<td>41</td>
</tr>
<tr>
<td>Number</td>
<td>36.9</td>
<td>63.1</td>
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<td></td>
</tr>
<tr>
<td>Absent</td>
<td>44</td>
<td>175</td>
</tr>
<tr>
<td>Number</td>
<td>20.1</td>
<td>79.9</td>
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<td>Percentage</td>
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<tr>
<td>Total</td>
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<td>216</td>
</tr>
<tr>
<td>Percentage</td>
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<td>76.1</td>
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**Table 4: Association between depression and HTDIS**

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<th>DEP</th>
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<tbody>
<tr>
<td></td>
<td>Absent</td>
<td>Present</td>
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<tr>
<td>Absent</td>
<td>212</td>
<td>31</td>
</tr>
<tr>
<td>Number (%)</td>
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<td>12.8</td>
</tr>
<tr>
<td>Present</td>
<td>30</td>
<td>11</td>
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<tr>
<td>Number (%)</td>
<td>73.2</td>
<td>26.8</td>
</tr>
<tr>
<td>Total</td>
<td>242</td>
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</tr>
<tr>
<td>Percentage</td>
<td>85.2</td>
<td>14.8</td>
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DEP: Depressive disorder, HTDIS: Hypertensive disorder in pregnancy, Chi-square=8.381, P=0.004
in pregnancy anxiety from different parts of the world reported a prevalence rate of 14-54%.\textsuperscript{9,19-21} However, the findings of our study are comparable with those reported in developing countries. In Brazil, the prevalence rate of anxious symptoms among pregnant women was estimated to be 60%, and the rate for depressive symptoms was about 20%.\textsuperscript{22} Furthermore, in Bangladesh, the prevalence rate of depressive symptoms among pregnant women was estimated to be 33% and 42.7% in Pakistan.\textsuperscript{23} The prevalence of anxiety (41%) and depression (57%) was found in Nicaraguan pregnant women.\textsuperscript{24}

Depressive and ANYAXs during pregnancy were strongly associated with the development of OBSDYs in the present study. Andersson \textit{et al.}\textsuperscript{18} analyzed the obstetric outcome and health-care consumption during pregnancy, delivery, and the early postpartum period in an unselected population-based sample of 1495 pregnant women diagnosed with antenatal depressive and/or ANYAXs, compared with healthy participants. Significant associations were found between depression and/or anxiety and increased nausea and vomiting, prolonged sick leave during pregnancy, and increased number of visits to the obstetrician, specifically, visits related to fear of childbirth and those related to contractions. Planned cesarean delivery and epidural analgesia during labor were also significantly more common in women with antenatal depression and/or anxiety.

Pathophysiological mechanisms to explain the factors responsible for adverse obstetrical outcomes in physically healthy women suffering from PSYDSs during pregnancy have focused on hormonal mechanisms to explain the findings.

Bonari \textit{et al.}\textsuperscript{14} in a review of perinatal risks of untreated depression concluded that depression in pregnancy was significantly associated with preterm delivery and growth retardation, preeclampsia, spontaneous abortion, and impaired perinatal development.

Andersson \textit{et al.}\textsuperscript{18} analyzed the obstetric outcome and health-care consumption during pregnancy, delivery, and the early postpartum period in an unselected population-based sample of 1495 pregnant women diagnosed with antenatal depressive and/or ANYAXs, compared with healthy participants. Significant associations were found between depression and/or anxiety and increased nausea and vomiting, prolonged sick leave during pregnancy, and increased number of visits to the obstetrician, specifically, visits related to fear of childbirth and those related to contractions. Planned cesarean delivery and epidural analgesia during labor were also significantly more common in women with antenatal depression and/or anxiety.

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Nadelson and Dickstein\textsuperscript{25} Kammnerer \textit{et al.},\textsuperscript{15} Mastorakos and Ilias\textsuperscript{26} Ochedalski and Lachowicz\textsuperscript{27} and Halbreich\textsuperscript{28} in five independent papers, have proposed several mechanisms which may interact to produce an adverse obstetric outcome. The neuroendocrine stress response, immunosuppression, and the role of genetics have been implicated as some of the mechanisms leading to OBSDYs.

Depression in pregnancy was found to be significantly associated with the development of hypertensive disorders in pregnancy. This finding is in accord with that of Kurki \textit{et al.}\textsuperscript{29} who found that depression and anxiety in early pregnancy were significantly associated with preeclampsia, and Evans \textit{et al.},\textsuperscript{1} who reported a significant association between depression in pregnancy and development of preeclampsia. However, Larsson \textit{et al.}\textsuperscript{30} did not find any association between depression and preeclampsia.

Depressive disorders may be harmful through an altered secretion of vasoactive hormones and other neuroendocrine transmitters. This may in turn cause vasoconstriction and
increased uterine artery resistance and, therefore, elevate blood pressure. Depressive disorders during pregnancy increase stress resulting in increased levels of pressor agents, i.e., epinephrine, norepinephrine, and angiotensin 2, Halbreich. An increased level of prostaglandins is seen during stress and may contribute to vasoconstrictor effects.

This immune response in early pregnancy is primarily a Th-1 response with the secretion of interferon-gamma, interleukin 2 (IL-2), and tumor necrosis factor-beta which promote cellular immunity. If the Th-1 response persisted beyond early implantation, the pregnancy may not survive; thus, there is a switch in the immune system to a Th-2 with a different set of cytokines, IL-4, IL-10, and IL-13 that promote humoral immunity and a decreased risk of rejection. However, depression and anxiety can cause an increase in the Th-2 response resulting in an inflammatory cascade and endothelial injury.

Further depressive disorder can cause an abnormal immunological reaction thus making the individual susceptible to infection.

Interestingly, the above mechanisms have also been postulated in the pathophysiology of preeclampsia. Hence, depression in pregnancy may increase susceptibility to preeclampsia by increasing stress.

ANYAXs in pregnancy were significantly associated with FGDs, i.e., small for gestational age babies. Dole et al. in a prospective cohort study of 1962 pregnant women in central North Carolina between 1996 and 2000, found a significant association between ANYAXs in pregnancy and preterm birth. Similarly, Kent et al. reported a significant association between ANYAXs in pregnancy and preterm birth. This could be explained on the basis of several mechanisms.

Placental CRH plays an important role in the communication between the placenta and the maternal and fetal adrenal gland for the production of precursors of estrogen production which are important for uterine growth and perfusion. First, elevations in CRH appear in the fetal circulation, as shown by Goland et al. suggesting that this peptide is available to activate the fetal pituitary-adrenal axis, which is considered to be mature during the second trimester. The relationship between maternal endocrine events, placental CRH, and the fetal pituitary-adrenal axis could be an attempt by the maternal-fetal-placental unit to bring about early fetal maturation to increase the chances for survival if delivered early, Hobel et al.

Anxiety in pregnancy is associated with increased uterine artery resistance as demonstrated by Texeira et al. This may reduce uteroplacental perfusion and exchange and contribute to intrauterine growth retardation.

Third, elevated levels of pituitary hormones such as oxytocin and prostaglandins may result in premature uterine contractions and contribute to the initiation of premature labor.

Furthermore, elevated stress levels resulting in immunosuppression may predispose to the development of infections, thus hampering fetal growth and causing prematurity.

Finally, patients with depressive and ANYAXs might be more likely to engage in poor health behaviors such as inadequate diet, or smoking, or might be less likely to avail adequate prenatal services. However, this factor was controlled for in the present study; it appears the findings in this study are more likely due to neuroendocrine parameters.

Although most studies have found a significant association between ANYAX in pregnancy and FGD, a large meta-analysis by Littleton et al. did not find any relationship between ANYAX and OBSDYSs.

The risk of preterm birth increased significantly in women who had a PSYDS compared to cohorts without a psychiatric diagnosis. Steer et al. found elevated risks for preterm delivery (<37 weeks), low birth weight (<2500 g), and babies small for their gestational age (<10th percentile) among women who had scores of 21 or more on the Beck Depression Inventory and who were not receiving active treatment.

The neuroendocrine disturbances described above possibly increase uterine irritability resulting in preterm labor and subsequent delivery.

Similarly, it was observed that women with PSYDSs were more likely to deliver babies with low Apgar score at birth. Apgar score is a measure of fetal distress due to a deleterious intraterine environment or birth trauma.

Chung et al. using serial ultrasonography demonstrated that the fetus of a mother suffering from depression spends more time in sleep and exhibits less body movement than the fetus of a mother without depression. A similar study by Allister et al. using ultrasonography suggested that maternal depression may affect fetal heart rate response to vibroacoustic stimulation. This test produces cardio acceleration typical of a healthy fetus and is commonly used to assess fetal well-being. In women with untreated depression, there was a delayed fetal response to a
vibroacoustic stimulus applied to the maternal abdomen. These findings are suggestive of fetal distress. Zax et al.28 and Patel et al.29 found significant associations between maternal depression in pregnancy and lower Apgar scores in the offspring. The causative factors may be placental insufficiency, prematurity, or superimposed infections.

CONCLUSION

The findings of this study suggest that contrary to popular belief, a substantial number of women suffer from PSYDSs in the antenatal period. Development of PSYDSs may precipitate OBSDYSs and thus jeopardize the course of pregnancy with adverse consequences both for the mother and developing fetus.

However, PSYDSs during pregnancy are under diagnosed, ignored, or undertreated. Routine assessment of the mental health of pregnant women at a primary healthcare level has the potential to identify early those women experiencing distress or with significant risk factors for perinatal disorders.

Clinicians, families, and women themselves need to be educated about the perils of untreated PSYDSs in pregnancy so that they can make truly informed treatment decisions.

Currently, the multiple clinical and research disciplines that are concerned with the various aspects of pregnancy, delivery, and postpartum period are not conceptually and practically integrated. Specifically, obstetricians are more concerned with delivery complications, whereas mental health professionals are concerned with the treatment of PSYDSs. An interdisciplinary approach is needed for better understanding of psychological processes and the development of measurements and interventions to prevent long-term impact on the offspring.

In the light of these findings, further research is necessary to determine the causal mechanisms by which PSYDSs result in OBSDYSs, as well as long-term effects on the mental health of children. In addition, studies are necessary to determine the optimum treatment of these disorders during pregnancy as well as effectiveness of psychosocial interventions.

LIMITATIONS OF THE STUDY

1. The study was carried out at a tertiary care hospital in Goa; hence, the findings cannot be extrapolated to the general population
2. As the primary focus of the study was to assess whether PSYDSs caused OBSDYSs, life events, and support systems that might influence the development and course of PSYDSs during pregnancy were not considered.

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Mitomycin - C Effect after Endonasal Endoscopic Sinus Surgery on Antrostomy Size

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Abstract

Introduction: Mitomycin-C (MMC) is an antibiotic and anti-neoplastic agent which decreases the scar formation along with production of fibroblast.

Aim: To know the effect of MMC on the antrostomy size.

Materials and Methods: (1) 40 patients of chronic sinusitis on both side, (2) after performing middle meatal antrostomy on anyone side a piece of mewal soaked in 1.5 ml of metomycine-c applied for five minute. On other side normal saline was applied for control, (3) the size of antrostomy was measured with a ruler after surgery.

Result: The effect of MMC in maintaining the antrostomy size was effective and the relative size was effectively more as compared with that of control side.

Conclusion: The patency of antrostomy side has significant effect after MMC topical application.

Key words: Middle Meatal Antrostomy, Mitomycin-C, Sinus Surgery

INTRODUCTION

Mitomycin-C (MMC) is an abstract from Streptomyces caespitosus which inhibits DNA, RNA, protein synthesis, and fibroblast proliferation resulting into hindrance in collagen synthesis.¹² MMC has been used in dacryocystorhinostomy as it adequately prevents obstruction of lacrimal duct by obstructing granular tissue formation.³⁻⁵ MMC has shown lower adhesion rate in middle meatus than in control site without MMC at completion of endonasal endoscopic sinus surgery.⁶ MMC application during surgery improves the post-operative result by preventing scar formation.

The aim of this study is to compare the result in surface area of antrostomy site between the control site and MMC applied side. The patency of antrostomy site is critical point for success rate of surgery. Post-operative adhesions and stenosis due to the formation of scar tissue and granulation during tissue recovery process.¹³⁻¹⁵ Attempts to decrease adhesion and stenosis after surgery includes packs, spaces and nasal splints are controversial.⁷⁻¹² Allergy, asthma, and nasal polyp are known factor to influence on success rate of endonasal endoscopic sinus surgery.¹³⁻¹⁵

MATERIALS AND METHODS

Materials

- Those patients who had similar score on both the sides on Lund-Macky scoring system as graded on C.T. PNS.¹⁶
- All of them had obstructed both ostiomeatal complex and various degree of opacification in both maxillary sinuses.
- The average age of patients was 30 years. (20-56 years).
- 28 male and 12 female.

Methods

- Every surgery was performed under general anesthesia.
- By performing endonasal endoscopic sinus surgery....
preservation of nasal mucosa was done as much as possible.
• After performing uncinectomy both maxillary sinuses were opened with back biting forceps and the redundant mucosa and polyps were trimmed with help of microdebrider.
• The anterior and superior portions of natural ostium were intact as circumferential cutting induce edema of mucosa antrum by preventing lymphatic drainage.
• Care was taken to preserve middle turbinate and its mucosa. The position of middle turbinate was maintained by preventing horizontal position of basal lamella.
• Random application of MMC at one side and normal saline on other side was done.

To measure surface area of antrostomy a rular with 1 mm unit wire gauge was designed. Using the rular one can measure the distance of horizontal and vertical axes of antrostomy site. The area was presumed to be oval in shape. The surface area was measured by calibration:

\[ \text{Surface area} = \pi \times a \times b/4, \]

\[ a = \text{horizontal value} \]

\[ b = \text{vertical value} \]

Before the application of MMC, 3 times measurement was done and mean measurement was used to minimize the error. Both the opening of antrostomy site was packed with merocel (Medtronic xomed) and one side 1.5 ml of MMC and other side 1.5 ml of normal saline was injected.

After 5 min, measurement size of antrostomy was done three times, and mean measurement was used. In post-operative care, use of oral antibiotics, steroids for four weeks and nasal irrigation for two months with NASOWASH were given. Post-operative dressing for removal of blood clots and crusts was done every 10th day for next 1½ months.

The measurement was done by same method at the end of 1st month, 3rd month, and 6th month postoperatively to compare the patency of antrostomies, we compare the average and relative sizes, i.e., the ratio of remaining antrostomy area with compare to immediate post-operative area between the two sides at each time after surgery.

Results

The closure and stenosis of antrostomy site was not different between the MMC side (closure 0 of 40 cases; Stenosis 2 of 40 cases) and control side (closure 4 of 40; Stenosis 4 of 40 cases) at 6 months after operation (fisher exact test \( P = 1.00 \)). In the immediate post-operative period, the average size of antrostomy was larger in control group than in MMC group (control versus MMC, 2.86 ± 0.72 cm² versus 2.55 ± 0.28 cm²; \( P > 0.05 \)).

But after 1 month, the sizes were reversed and the area was larger in MMC group than in control group (control versus MMC, 1.35 ± 0.51 cm² versus 1.72 ± 0.23 cm²; \( P = 0.1 \)). Moreover, the average antrostomy size was greater in MMC group at 3rd month and 6 month.

The relative size (percent; the ratio of remaining antrostomy area compare to the area immediately after operation) of antrostomy site at 1 month compare to the initial size was significantly increased in MMC group as compare to control group (control versus MMC group 47.2% ± 15.2% versus 67.4% ± 10.1%; \( P = 0.017 \)).

The relative size at third month and six month was also greater in MMC group but the difference was not statistically significant. The effect of MMC in maintaining size of antrostomy was more after 1 month of surgery (Figure 1).

Discussion

The study done by Chung et al. shows that MMC application causes lower incidence of middle meatus addition as compare to control side, but my result shows that application of MMC does not decrease the incidence of stenosis and closure of antrostomy after six months.5 Although MMC may have only short term effect.6 Infection following endonasal endoscopic sinus surgery affect the occurrence of antrostomy stenosis or closure in patients.

The relative size of antrostomy site applied with MMC is greater (67.4%) as compare to control group (47.2%) after surgery. Middle meatal antrostomy stenosis is not the only cause for failure of surgery but is a common one. Scarring and addition of maxillary sinus ostium and ethmoid sinus were only endoscopic finding that correlated to poor outcome of sinus surgery.7

Salam and Cable classified the patency of middle meatal antrostomy after surgery into four groups: Widely patent (more than 8 mm), patent (5 to 8 mm), stenosed (<5 mm),
Kumar and Verma: Mitomycin-C Effect on Antrostomy Size

and blocked by mucosal disease. They reported that there is a significant relationship between the degree of patency and degree of improvement of symptoms of chronic maxillary sinusitis.

Albu and Tomescu compared small (<6 mm) antrostomies with large (more than 16 mm) antrostomies in relieving symptoms of chronic maxillary sinusitis, also found that antrostomy sized has no influence on outcome of surgery for maxillary sinusitis.

My study is different from previous studies in many ways. The method for measuring antrostomy sized only with an endoscopy is in accurate and chances of error will be due to endoscopic visuospatial distortion.

Nouraei et al. introduce a 5 mm probe in conjunction with software use on computer. We measured size of antrostomy with right angled ruler which is marked at 1 mm intervals, which can measure superior-inferior axis and anterior-posterior axis too. The effect of MMC on fibroblast is to inhibit proliferation and scar formation and to delay fibrosis to let epithelium re-epithelialize before a scar forms. Local infiltration of small amount of MMC does not induce general toxicity. MMC at 1 mg/ml also shown a cytotoxic effect on cultured fibroblast and the effect of decreasing cultured cell numbers.

MMC treated success rate of dacryocystorhinostomy in patients were 94-100%. Even in repeat dacryocystorhinostomy the application of MMC has been reported successfully. MMC used as an adjuent for patients with vocal fold and tracheal stenosis during endoscopic laser surgery. In summary, this study demonstrates application of MMC on antrostomy did not decrease the incidence of stenosis and closure but was effective in maintaining antrostomy size.

CONCLUSION

The application of MMC at antrostomy site may be effective adjunt therapy in maintaining the patency of size of antrostomy in early postoperative period.

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Kumar and Verma: Mitomycin-C Effect on Antrostomy Size


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Assessment of Vitamin D Deficiency in Pregnant Females Attending Antenatal Care Clinic at Tertiary Care Hospital

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Abstract

Introduction: Vitamin D deficiency during pregnancy is associated with increased maternal risks such as pre-eclampsia, gestational diabetes mellitus, and bacterial vaginosis as well as a higher incidence of fetal complications such as low birth weight, neonatal rickets, and osteoporotic fracture in late adulthood.

Objective: To find the prevalence of vitamin D deficiency in pregnant females attending antenatal care clinic in tertiary care hospital and to evaluate other related risk factors associated with vitamin D deficiency.

Materials and Methods: This study was conducted in the Department of Obstetrics and Gynecology, SMIMER, Surat. Total 253 pregnant females were randomly selected who attended antenatal clinic from December 2014 to December 2015. Women with serum 25-hydroxy vitamin D level <20 ng/ml were diagnosed as vitamin D deficient.

Results: In this study, out of 253 cases, 211 cases (83.4%) had vitamin D deficiency (vitamin D <20 ng/ml), 28 cases (11.1%) had insufficiency (vitamin D = 21-29 ng/ml), and only 14 cases (5.53%) had sufficient vitamin D levels (vitamin D ≥30 ng/ml).

Conclusion: This study indicates that vitamin D deficiency is highly prevalent in pregnant females thus implicating the need of a uniform strategy to give vitamin D supplements to all pregnant females.

Key words: Maternal serum 25 hydroxy vitamin D, Vitamin D deficiency, Vitamin D insufficiency, Vitamin D supplementation in pregnancy

INTRODUCTION

Vitamin D deficiency is a preventable health problem. As calcium demands increase during pregnancy, vitamin D status becomes crucial and optimal for maternal and fetal outcome. Vitamin D deficiency during pregnancy may lead to increase the risk of pre-eclampsia, gestational diabetes mellitus (GDM), bacterial vaginosis, and more chances of cesarean section. Low levels of vitamin D are also linked with a number of fetal health problems such as low birth weight, neonatal hypocalcemia and seizures, impaired growth, skeletal problems such as rickets and low bone mineral density and also acute lower respiratory tract infections.

The main action of vitamin D is to maintain the physiological levels of serum calcium and phosphorus. There are two main sources of vitamin D-(1) exogenous source from the diet in the form of vitamins D2 and D3 and (2) endogenous source in the form of vitamin D3 (cholecalciferol) is synthesized in the skin by the action of sunlight. Endogenous vitamin D is the main source in children and adults, thus any factor affecting the transmission of ultraviolet B radiation will determine the reduction of vitamin D-25 hydroxy vitamin D. Excessive use of sunscreens, individuals with darker skin, skin aging, and skin damage secondary to burns are some of the risk factors which may cause decrease in endogenous

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production of vitamin D. Other causes of vitamin D deficiency can be inadequate intake, obesity, severe liver failure, drugs such as anticonvulsants and glucocorticoids.

During pregnancy and lactation, significant changes in calcium and vitamin D metabolism occur to meet the increased demand of calcium needed for fetal bone mineralization. Women of Indian origin especially pregnant women have a high prevalence of vitamin D deficiency. In Indian women, calcium intake is low and demand of calcium is high because of repeated cycles of pregnancy and lactation. Low calcium intake in conjunction with vitamin D deficiency makes the condition worse. Thus, the need for improvement in vitamin D status in pregnant females is both important and urgent.

**MATERIALS AND METHODS**

This cross-sectional study was conducted in the Surat Municipal Institute of Medical Education and Research in the Department of Obstetrics and Gynecology. Total of 253 participants were randomly selected from pregnant females attending antenatal care clinic from December 2014 to December 2015. Pregnant females who gave voluntary consent were included in the study, irrespective of the period of gestation. Women with renal disease, chronic liver disease, and patient taking antitubercular drugs or antiepileptic drugs were excluded from the study. The study was approved by the Institutional Ethical Committee. Apart from routine history and examination, patients’ blood samples were collected for serum 25-hydroxy vitamin D level estimations, apart from routine investigations.

Women with serum 25-hydroxy vitamin D level <20 ng/ml were diagnosed as vitamin D deficient; levels between 21 and 29 ng/ml were diagnosed as vitamin D insufficient, and levels ≥30 ng/ml were considered sufficient.

**RESULTS**

In this study, out of 253 cases, 211 cases (83.4%) were diagnosed as vitamin D deficient, 28 cases (11.1%) were diagnosed as vitamin D insufficient, and only 14 cases (5.53%) were found to have sufficient vitamin D levels (Table 1). Thus, the prevalence of vitamin D deficiency and insufficiency in pregnant females in this study was 94.47%.

Vitamin D deficiency and insufficiency were prevalent in almost all age groups studied. Out of 97 primigravida, 78 cases (80.41%) were vitamin D deficient, and out of 156 multigravida, 133 cases (85.26%) had vitamin D deficiency. So, there was a high distribution of vitamin D deficiency in both primi- and multi-gravida. In our study, the prevalence rate of vitamin D deficiency was much higher in lower socio-economic class (64 cases [94.12%] out of 68) as compared to upper socio-economic class (1 case [25%] out of 4). We also observed that vitamin D deficiency was equally prevalent in all trimester of pregnancy. Out of 13 cases of first trimester, 11 subjects (84.62%) were deficient and 2 subjects (15.38%) were insufficient. Out of 49 cases of second trimester, 41 cases (83.67%) were deficient and 6 cases (12.4%) were insufficient for vitamin D. Similarly, from 191 cases of third trimester, 159 cases (83.25%) were vitamin D deficient, and 20 cases (10.47%) were vitamin D insufficient.

As shown in Table 2, a strong correlation was seen between increasing body mass index (BMI) and vitamin D deficiency and insufficiency. All obese females, i.e., BMI ≥30 were found to have vitamin D deficiency (100% prevalence).

In this study of 253 cases, 86 cases had anemia, in which 74 cases (86.1%) had vitamin D deficiency, and 9 cases (10.47%) had vitamin D insufficiency. Total 14 cases of pregnancy-induced hypertension were diagnosed, of which 13 cases (92.86%) had vitamin D deficiency and 1 case (7.14%) had vitamin D insufficiency. GDM was found in 6 cases, of which 5 cases (83.33%) were deficient for vitamin D (Table 3).

**DISCUSSION**

In our study, a very high prevalence of vitamin D deficiency (83.4%) and insufficiency (11.1%) was found.
among pregnant females. This may be due to higher skin pigmentation, vegetarian diet, and inadequate intake. Our results are comparable to the study conducted by Sharma et al.,\(^1\) who found that the prevalence of vitamin D deficiency in pregnant females in North Indian population was 93%. The prevalence of vitamin D deficiency was comparatively lesser in studies conducted by Ravinder et al.,\(^2\) Vandevijvere et al.,\(^3\) and Bartoszewicz et al.\(^4\) (Table 4). Vitamin D deficiency and insufficiency were found to be higher in multigravida as compared to primigravida. This could be due to repeated cycles of pregnancy and lactation in multigravida. Choi et al.\(^5\) observed that in primigravida, severe vitamin D deficiency was present in 75.4% cases, and in multigravida, vitamin D deficiency was present in 80.8% cases.

As far as the trimester of pregnancy was concerned, vitamin D deficiency was prevalent in all trimester. In this study, the prevalence rate of vitamin D deficiency was much higher in lower socio-economic class as compared to upper socio-economic class. This could be because of poor dietary intake in lower economic strata.

A very important correlation was found between vitamin D deficiency and increasing BMI in our study. This can be possibly due to the sequestration of vitamin D in adipose tissue and its lower dietary intake. Bodnar et al.\(^6\) (2007) concluded in his study that 61% of women who were obese (BMI >30) before pregnancy were found to be vitamin D deficient as compared to 36% of women with pre-pregnancy BMI of <25.

**CONCLUSION**

As calcium demand increases during pregnancy, vitamin D status becomes crucial for optimal maternal and fetal outcome. The high prevalence of vitamin D deficiency in pregnancy calls for unanimous approach to tackle this grave situation by implementing a national strategy for screening, prevention, and treatment of this deficiency. Programs need to be developed to increase the awareness of this problem among people and to provide adequate doses of vitamin D supplements to pregnant females to avoid maternal and fetal complications which may occur due to vitamin D deficiency.

**REFERENCES**

Low-dose Versus High-dose Statin Therapy for Prevention of Post-operative Atrial Fibrillation in Off-pump Coronary Artery Bypass Grafting - A Prospective, Randomized, Control Trial

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Abstract

Background: Statins are commonly used medications during a post-operative period for off-pump coronary artery bypass grafting cases. American College of Cardiology/American Heart Association guidelines specifically address the issue with recommending use of post-operative statin. However, do not mention specific dosages. The role for prevention of long-term mortality secondary to cardiovascular events is well studied, though dosages are unclear. We tried to address this issue looking specifically whether low-dose or high-dose statins are useful for prevention of post-operative atrial fibrillation (AF).

Aims and Objectives: To assess the impact of the use of low-dose versus high-dose statin for prevention of AF in immediate post-operative period in patients undergoing off-pump coronary artery bypass grafting.

Materials and Methods: This was prospective, randomized, control trial conducted for 1 year between tertiary care cardiac surgical units. A total 120 patients were enrolled in the study; both the groups received similar pre-operative medications. Intraoperative patients were randomized to receive low-dose (20 mg) versus high-dose (80 mg) atorvastatin. From second post-operative day, the same dose was continued until the end of the 1st month. The primary outcome variable was the incidence of post-operative AF. Secondary outcome variables were major adverse cardiac and cerebrovascular events and persistence of AF at 1 month.

Result: A total of 120 patients included in the study. Demographic profile and risk factors were similar in both the groups. Post-operative AF was observed in 2 patients in Group A and 3 patients in Group B with non-significant $P$ values. Major cardiac adverse effects were observed in 1 patient in each group. While no patient continued to have post-operative AF at the 1st month follow-up.

Conclusion: Both low-dose and high-dose statins are equally effective in treating post-operative AF.

Key words: Atorvastatin, Atrial fibrillation, Low dose, Off-pump coronary artery bypass grafting, Statins

INTRODUCTION

Atrial fibrillation (AF) is one of the types of supraventricular tachyarrhythmia characterized by uncoordinated atrial activation with ensuing worsening of cardiac function. Post-operative AF (POAF) is more common than before due to the greater than before number of cardiac surgeries being performed in Indian patients. This consecutively is associated with an increased incidence of post-operative complications, length of hospital stay, and later increase in the cost of hospitalization. Therefore, preventing and/or minimizing AF by pharmacological or non-pharmacological means is a reasonable objective.\(^1\)\(^2\) AF has been reported in up to 5-40% of patients in the early post-operative period following coronary artery bypass graft (CABG).\(^3\)\(^5\) AF worsens patient’s hemodynamic status and increases the risk of congestive heart failure, embolic events, and longer Intensive Care Unit stays.

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Statins are highly effective in lowering serum cholesterol concentrations through 3-hydroxy-3-methyl glutaryl coenzyme A reductase inhibition and thus are vital to the primary and secondary prevention of cardiovascular disease. More than 50% of patients undergoing major vascular surgery and 80% undergoing cardiac surgery are on chronic statin therapy. Statins also exert numerous lipid-independent or “pleiotropic” effects that were not expected during drug development due to their ability to inhibit the inflammatory response, reduce thrombosis, enhance fibrinolysis, decrease platelet reactivity, inhibit cell growth, reduce ischemia-reperfusion injury, and restore endothelial function. These beneficial effects result mainly from the modulation of the complex interplay between the pathologic triad of inflammation, dynamic obstruction, and thrombosis.6

2011 American College of Cardiology Foundation (ACCF)/American Heart Association (AHA) guideline for coronary artery bypass graft surgery. A report of the ACCF/AHA Task Force on Practice Guidelines states that all patients undergoing CABG should receive statin therapy unless contraindicated (level of evidence is A). These guidelines do not mention the dose of statin. Various dosages of atorvastatin are in use which range from low dose 20 mg/day to high dose which is 80 mg/day. ACC/AHA does not recommend any dose because exactly at what dose benefit occurs is still obscure.

In view of high morbidity with the development of AF, the treatment of it is constantly evolving with multimodal approach, and still, it is not possible to control it precisely. Many studies with statin therapy in Western scenario show conflicting results and overall trend toward protection. However, because of obvious epidemiological reasons, the same cannot be generalized for Indian patients, and there are no studies which compare dose of atorvastatin for Indian population for prevention of AF, so we decided to conduct a randomized control trial for the same in Indian population (Table 1).

**MATERIALS AND METHODS**

This was prospective, double-blind, parallel group, randomized, clinical trial of assessment of high-dose atorvastatin (80 mg) versus low-dose atorvastatin (20 mg) on post-operative AF in 120 cases who underwent elective off-pump CABG. The study protocol was approved by the Ethical Committee of the Institute (Table 2). Written valid and informed consent was obtained from all the patients before the procedure. Inclusion criteria included all patients posted for elective off-pump coronary artery bypass surgery. Exclusion criterion included active liver disease.

<table>
<thead>
<tr>
<th>Table 1: Patients characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Variable</td>
</tr>
<tr>
<td>Age in years</td>
</tr>
<tr>
<td>Male sex</td>
</tr>
<tr>
<td>Ejection fraction</td>
</tr>
<tr>
<td>Number of diseased vessels</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Table 2: Risk factor of the patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Variable</td>
</tr>
<tr>
<td>NYHA grade 2 angina</td>
</tr>
<tr>
<td>Hypertension</td>
</tr>
<tr>
<td>Diabetes</td>
</tr>
<tr>
<td>Old myocardial infarction</td>
</tr>
<tr>
<td>Old cerebrovascular accident</td>
</tr>
</tbody>
</table>

NYHA: New York Heart Association

Patients were identified by primary investigator 1 day before surgery in pre-anesthesia clinic. Aspirin and clopidogrel were stopped 5 days before surgery while calcium channel blockers, angiotensin-converting enzyme inhibitor or angiotensin receptor blockers were stopped 1 day before surgery as per institutional protocol. Beta blockers and nitroglycerines were continued. All pre-operative dose of atorvastatin was continued which is 20 mg as institutional protocol.

Intraoperatively, after bypass grafting is over, 80 mg atorvastatin was given in one group of patients (Group A) while no atorvastatin was given in Group B through Ryles tube. After extubation, from 2nd day, Group A patients received atorvastatin 80 mg/day while Group B received atorvastatin 20 mg/day. Demographic characteristics of the patients were collected.

Primary outcome variable was the incidence of post-operative AF. Secondary outcome variables were major adverse cardiac and cerebrovascular events, and persistence of AF at 1 month.

**Statistical Analysis**

Data expressed at mean ± standard deviation. Student’s t-test was applied to compare study Groups A and B. Paired t-test was used to compare variable before and after the intervention value <0.05 was considered significant. SPSS 19 was used for statistical analysis.

**RESULTS**

A total of 120 patients included in our study which was done from June 2015 to June 2016. Mean age in years was 56 ± 10 years in Group A while Group B it was 57 ± 12 years. 56 were male in Group A while 54 were
male in Group B. Mean ejection fraction was 52 ± 12 in Group A while 51 ± 10 in Group B. Number of diseased vessels in Group A was 2.4 versus 2.2 in Group B.

When we compared risk factors, New York Heart Association class 2 angina was present in 50 cases in Group A while in 54 cases in Group B. Hypertension was present in 72 cases in Group A while in 74 cases of Group B. Previous myocardial infarction was present in 42 cases in Group A while 46 cases of Group B. Previous cerebrovascular accident was present in 10 cases of Group A while 12 cases of Group B. P values are shown in respective tables and are non-significant.

POAF occurred in 2 cases in Group A while it occurred in 3 cases in Group B. The p value was 0.23 which is non-significant. One case each of major adverse cardiac event occurred in each group with a non-significant P value. While no patient persisted with AF at the end of 1 month.

**DISCUSSION**

The use of statins in perioperative period now is mandatory as supported by various trials and suggested by ACC/AHA guidelines.7-11 Statins have got additional beneficial effects which include anti-inflammatory effects, plaque stabilization effect, and antioxidant effect. Advanced data also suggest beneficial effect on mortality and morbidity. The question remains unanswered is what is exact dose? Are low-dose statins useful or high-dose statins should be given? Our prospective, randomized, control trial shows that the incidence of post-operative AF, major adverse cardiac event, and AF at the end of the 1\textsuperscript{st} month is equal in low-dose versus high-dose statin group indication efficacy for even a lower dose of atorvastatin in the 1\textsuperscript{st} month postsurgery.

Two studies\textsuperscript{11,12} specifically look after low-dose versus high-dose atorvastatin therapy after coronary artery bypass grafting. Compared with the less aggressively treated patients, those in the atorvastatin 80-mg group experienced a 27% reduction in major cardiovascular events and a 30% reduction in repeat coronary revascularization (either CABG or percutaneous coronary intervention) during a mean follow-up of 4.9 years. The number needed to treat with 80 mg compared with 10 mg to prevent 1 of these events was 16 in both the studies.

Although above studies look at different parameters after cardiac surgery, no study specifically looks at AF prevention which is the primary goal of our study (Table 3).

Our study specifically looks at reduction of post-operative AF and statistically proves that AF can be prevented by both the low-dose and high-dose statins effectively. However, when we see from a broader perspective in view of reduction in long-term mortality and morbidity, it should be concluded that higher doses are safer in view of secondary beneficial effects, while initial period for prevention of hospital costs and patient morbidity, both dosages can be used.\textsuperscript{13}

**CONCLUSION**

Low-dose and high-dose statins are equally effective for immediate prevention of post-operative AF.

**LIMITATION OF THE STUDY**

The study has got several limitations. First, it specifically looked into a single parameter, i.e., AF in view of hospital costing as a post-operative morbidity rather than taking a holistic approach for post-operative mortality reduction. The second limitation is data are not collected regarding cholesterol levels of the patients.

**REFERENCES**


How to cite this article: Mudgalkar NN. Low-dose Versus High-dose Statin Therapy for Prevention of Post-operative Atrial Fibrillation in Off-pump Coronary Artery Bypass Grafting - A Prospective, Randomized, Control Trial. Int J Sci Stud 2016;4(5):102-105.

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Prognostic Importance of White Blood Cell Count and Plasma Glucose Levels at Admission in Acute Myocardial Infarction

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Abstract

Introduction: An increase in white blood cell (WBC) count and a high plasma glucose level are frequently observed in patients with acute myocardial infarction. WBC count is a simple marker of inflammation, which plays an important role in acute coronary syndrome. It is seen that WBC count plays a potential role in promoting blood coagulation, mediating microvascular reflow, and causing myocyte dysfunction.

Materials and Methods: About 100 consecutive patients presenting with acute myocardial infarction admitted to New Civil Hospital, Surat, from September 2014 to September 2015 were studied. The study were carried out on patients presenting with complains suggestive of acute myocardial infarction presenting within 48 h in Emergency Department of New Civil Hospital, Surat. After the patient was stabilized, qualifying patients underwent detailed history and clinical examination. The WBC count and plasma glucose levels were measured at the time of admission.

Results: In present study, 36 (36%) out of 100 patients were found to be dyslipidemic and prior ischemic heart disease about 12 (12%) out of 100.

Conclusion: WBC count and plasma glucose level at admission has a prognostic importance as independent and joint variables in predictors for short-term outcome in the form of in-hospital mortality in acute myocardial infarction cases.

Key words: Acute Myocardial Infarction, Plasma Glucose, White Blood Cell

INTRODUCTION

An increase in white blood cell (WBC) count and a high plasma glucose level are frequently observed in patients with acute myocardial infarction. WBC count is a simple marker of inflammation, which plays an important role in acute coronary syndrome. It is seen that WBC count plays a potential role in promoting blood coagulation, mediating microvascular reflow, and causing myocyte dysfunction.¹,²

In addition, a high blood glucose level has been associated with an increased risk of mortality and morbidity in patients with acute myocardial infarction, regardless of their diabetic status. Acute hyperglycemia can induce oxidative stress and activate coagulation, endothelial dysfunction, and inflammation. Therefore, both inflammation and hyperglycemia have at least partly similar pathogenic mechanisms that might increase myocardial injury.³,⁴

Although predictive utility of an elevated WBC count and hyperglycemia in relation to survival after acute myocardial infarction have been studied independently, but a joint study of WBC count and blood glucose levels together in predicting in-hospital outcomes is lacking.⁷

Purpose

This study is done to know the prognostic importance of WBC count and blood glucose at admission in acute myocardial infarction.
MATERIALS AND METHODS

About 100 consecutive patients presenting with acute myocardial infarction admitted to New Civil Hospital, Surat, from September 2014 to September 2015 were studied.

Sample size has been calculated with OpenEpi Software with prevalence rate of congenital heart disease in India of 13.2% at a permissible error of 8%, so the size of sample works out to be 119, i.e., \( n = 119 \), out of which 19 patients denied to be the part of study.

The study were carried out on patients presenting with complains suggestive of acute myocardial infarction presenting within 48 h in Emergency Department of New Civil Hospital, Surat. After the patient was stabilized, qualifying patients underwent detailed history and clinical examination. The WBC count and plasma glucose levels were measured at the time of admission.

Inclusion Criteria
All acute myocardial infarction patients having:
1. Chest pain lasting more than 20 min
2. Diagnostic electrocardiogram (ECG) changes with characteristic ECG alterations consisting of new pathological Q waves or ST segment and T wave changes
3. Elevated creatine kinase MB levels >2 times the upper limit of normal.

Exclusion Criteria
All patients who did not fulfil the inclusion criteria.

Study End Points and Definitions
The primary end point of the study is all cause mortality during the period of stay in the hospital. Plasma glucose is the nonfasting glucose level measured at the time of admission. It is estimated by glucose oxidase glucose peroxidase technique.

Statistical Method
Data entered in MS Excel Spreadsheet and analyzed with the help of OpenEpi and SPSS V.16 software.
1. Descriptive statistics explained by frequency and percentage
2. Categorical variable explained by Chi-square test (test of significance)
3. Continuous variable explained by \( t \)-test and ANOVA (test of significance).
4. Multivariate analysis tests to determine the association between WBC count and blood glucose levels with in hospital mortality.

RESULTS

Results are been depicted in form of tables and graphs below (Tables 1-3), (Graphs 1-3).

Multivariate analysis showed that plasma glucose levels and WBC count are independent predictors of in-hospital mortality.

DISCUSSION

When a combination of these two variable, i.e., WBC count and plasma glucose levels were taken, we found that there is an increased mortality in patients who had a high WBC count and high glucose levels compared to...

The comparison of WBC count and glucose levels with left ventricular ejection fraction of those patients who survived showed a stepwise decrease in predischarge left ventricular ejection fraction. In a study done by Ishihara et al.,1 in 2006, there was a total of 218 deaths (5.9%). The patients with a high WBC count had a two-fold increase in hospital mortality compared with those with a low WBC count and patients with high glucose level had a 2.7-fold increase in mortality compared to the low plasma glucose level. When a combination of different strata for each variable was made, it showed that patients with a high WBC count and high plasma glucose levels had the highest risk compared with those with low WBC and low plasma glucose level. Moreover, in another study done in 2005, the patients with high WBC count and high glucose level were found to have a higher risk of mortality compared to the above study (18% vs. 11.8%). It described a 9.4-fold higher mortality in patients with high WBC count and high glucose level at admission compared to those with low values. In present study 18% (18 out of 100) cases found to be diabetic. As insulin deficiency hampers lipid metabolism and increases the amount of lipid, mainly free fatty acids in circulation. It also causes microangiopathies leading to impaired perfusion to target organs. Mechanism leading to accelerated atherosclerosis is hyperlipidemia along with increase in glycosaminoglycans.9,10

In present study, 36 (36%) out of 100 patients were found to be dyslipidemic and prior ischemic heart disease about 12 (12%) out of 100.

**CONCLUSION**

WBC count and plasma glucose level at admission has a prognostic importance as independent and joint variables in predictors for short-term outcome in the form of in-hospital mortality in acute myocardial infarction cases.

This study used simple variables such as plasma glucose levels and WBC count to predict near future consequences in a patient with myocardial infarction and vital interventions should be done at apt time.

**Table 1: Relation between risk factors and in-hospital mortality in glucose group**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Low (&lt;133 mg/dl) n=4</th>
<th>Med (133-182 mg/dl) n=4</th>
<th>High (&gt;182 mg/dl) n=10</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>59.3+11.1</td>
<td>63+10.4</td>
<td>58.18+11.9</td>
<td>More than 0.05</td>
</tr>
<tr>
<td>Diabetes</td>
<td>0</td>
<td>1</td>
<td>7</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Hypertension</td>
<td>0</td>
<td>1</td>
<td>8</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Smoker</td>
<td>0</td>
<td>3</td>
<td>7</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

**Table 2: Relation of the risk factors and in-hospital mortality in WBC count group**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Low WBC (&lt;8300) n=1</th>
<th>Med WBC (8300-11,000) n=5</th>
<th>High WBC (&gt;11,000) n=12</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>50.8+8.1</td>
<td>52+11.4</td>
<td>60.8+10.1</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Diabetes</td>
<td>0</td>
<td>1</td>
<td>9</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Hypertension</td>
<td>0</td>
<td>1</td>
<td>7</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Smoker</td>
<td>0</td>
<td>4</td>
<td>9</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Prior IHD</td>
<td>0</td>
<td>1</td>
<td>10</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Killip Class&gt;2</td>
<td>1</td>
<td>0</td>
<td>7</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>ST segment elevation</td>
<td>0</td>
<td>3</td>
<td>10</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Thrombolysis</td>
<td>0</td>
<td>1</td>
<td>9</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

**Table 3: Multivariate analysis assessing predictors for in-hospital mortality**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Chi-square</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kilip class</td>
<td>62.495</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Age</td>
<td>2.57</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>WBC count</td>
<td>8.67</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Plasma glucose</td>
<td>4.94</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Prior IHD</td>
<td>30.017</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Smoker</td>
<td>0.98</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Diabetes mellit</td>
<td>15.229</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Hypertension</td>
<td>4.15</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>ST elevation</td>
<td>6.24</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Thrombolysis</td>
<td>0.36</td>
<td>&gt;0.05</td>
</tr>
</tbody>
</table>

WBC: White blood cell, IHD: Ischemic heart disease
REFERENCES


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Histopathology of Liver in Diabetes Mellitus - An Autopsy Study

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Abstract

Background: Non-alcoholic steatohepatitis has been a well-known entity in association with Type 2 diabetes mellitus (DM) following insulin resistance and absence of overt hepatic manifestation. We aimed to study the histopathological features of liver in autopsy cases of known DM and identify the significant features and evaluate the extent of hepatic fibrosis seen in DM.

Materials and Methods: Liver histology of 86 autopsy cases of known DM was analyzed over a period of 6½ years with age- and sex-matched controls. Cases with overt hepatic diseases and alcohol intake were excluded from the study. Clinical and biochemical data were acquired from hospital records. Histological features were analyzed using non-alcoholic fatty liver disease scoring system.

Results: Steatosis, lobular and portal inflammation, nuclear glycogenation, and fibrosis were found to be significant features as compared to the controls.

Conclusion: Fibrosis appeared to be the independent feature irrespective of the degree of steatohepatitis, thus contributing to morbidity and mortality among diabetics.

Key words: Autopsy, Liver histopathology, Non-alcoholic fatty liver disease, Type 2 diabetes mellitus

INTRODUCTION

Non-alcoholic fatty liver disease (NAFLD) has been the most common liver disease in the developed world associated with risk factors such as obesity, Type 2 diabetes mellitus (DM), and dyslipidemia, and it is currently emerging as an epidemic in the developing nations as well. Urbanization and changes in lifestyle appear as the key factors for the development of NAFLD/non-alcoholic steatohepatitis (NASH), thus leading to an upsurge in the incidence of this metabolic syndrome. The rates in Asia-pacific region have been estimated to be 12-24% of the general population.¹ Among various factors leading to NAFLD, Type 2 DM appears to be an important factor as there is a rising concern over increasing insulin resistance following chronic liver disease due to NAFLD. In the literature, a high incidence of NAFLD is seen in diabetics, and Type 2 DM appears to be the independent risk factor for NAFLD. The histological spectrum of NAFLD comprises steatosis, steatohepatitis, fibrosis, and cirrhosis; changes resembling like alcoholic liver disease. Hence, the exclusion of history of alcohol consumption is essential for the diagnosis of NAFLD.

Newer imaging modalities and biomarkers are emerging as non-invasive methods for identifying NAFLD. However, histology continues to remain the gold standard for identifying the extent of liver disease. In the literature, this aspect has been assessed mainly on liver biopsies. We aimed to study the liver histology of autopsy cases of known Type 2 DM, identify the significant histological features, and evaluate the extent of fibrosis associated with morbidity and mortality.

MATERIALS AND METHODS

Autopsy records over a period of 6½ years from January 2001 to June 2007 were reviewed. From a total of 2542
autopsies, 86 adult autopsies of known Type 2 DM without any obvious liver disease were included in the study. Clinical and biochemical data were obtained from the hospital records. Cases with any previous history of liver disease or alcohol intake were excluded from the study. 55 age- and sex-matched autopsy cases with no history of Type 2 DM or any other liver disease were selected as controls. At least two hematoxylin and eosin (H and E) stained histological sections of liver were studied for both cases and controls.

The histological features of NAFLD identified were based on the NAFLD scoring system as described in the literature. These included grades of steatosis, lobular and portal inflammation, ballooning of hepatocytes, and nuclear glycogenation. Fibrosis was staged from 1 to 4 on the basis of its extent and location, i.e., portal, portal and periportal, bridging, and cirrhosis. Special stains such as Masson trichrome were used to identify stage 1a (pericellular) fibrosis. The results obtained were statistically analyzed using Fisher's test and \( P < 0.05 \) was considered significant.

**RESULTS**

Of the 86 autopsy cases with known Type 2 DM reviewed retrospectively for the changes of NAFLD in liver sections, 57 (66.3%) were males and 29 (33.7%) were females. Thus, males outnumbered females with a male:female ratio of 1.9:1. These 86 patients ranged in the age from 33 to 90 years, with mean age being 54.4 years. In majority of the cases, 49 (56.8%) were between 41 and 60 years (Figure 1).

**Hepatic Histology**

The histological features were identified using the NAFLD scoring guidelines in both cases and controls. Steatosis was seen in 34 (39.5%) cases. Of these, 13 (15.1%), 11 (12.7%), and 10 (11.6%) cases, respectively, showed Grade 1 (5-33%), Grade 2 (33-66%), and Grade 3 (>66%) steatosis. Eight (14.5%) cases out of 55 controls also showed features of steatosis, all of them being of Grade 1.

Lobular inflammation of Grade 1 (<2 foci/×20 field) was observed in majority of 42 (48.8%) cases followed by Grade 0 (no inflammatory foci), Grade 2 (2-4 foci/×20 field), and Grade 3 (>4 foci/×20 field) in 22 (25.5%), 14 (16.2%), and 8 (9.3%) cases, respectively. Portal inflammation was significantly observed in 54 (62.7%) cases, which was Grade 1 (>minimal) as against 32 (37.2%) cases of Grade 0 (none to minimal). The type of inflammation was predominantly of mononuclear cells comprising lymphocytes and plasma cells.

Although ballooning degeneration was observed in only 39 (45.3%) cases, it was still significant as compared to 3 (5.4%) cases among the controls. Nuclear glycogenation of hepatocytes was significantly observed in 59 (68.6%) cases as against none observed in the control cases.

Fibrosis was significantly observed in 34 (39.5%) cases as compared to the controls. Majority of the cases, i.e., 16 (18.6%) showed stage 2 (portal and periportal) fibrosis followed by 10 (11.6%) cases of stage 3 (bridging fibrosis), and 4 (4.6%) cases showed stage 4 fibrosis.

Statistical analysis of all the above-mentioned histological features by applying Fisher’s test showed them to be significant (\( P < 0.05 \)) in cases studied as compared to the controls (Table 1).

Out of 34 cases of fibrosis, 14 (41.1%) cases showed stage 3 and 4 fibrosis. Majority of these 14 cases had Grade 0 to 1 steatosis and lobular inflammation (Figure 2). Masson’s trichrome performed on liver sections did not identify additional cases with fibrosis.

**DISCUSSION**

The relationship between insulin resistance and liver disease has been well documented in literature.\(^2,3\) Insulin resistance is the central pathogenic mechanism in the development of both Type 2 DM and NASH.\(^4\) Harrison et al.\(^5\) have even described a type of diabetic microangiopathy affecting the liver apart from steatohepatitis.

This study was aimed mainly to study liver histopathology in autopsy cases of Type 2 DM and to identify histological...
features significantly associated with diabetes as compared to non-diabetic controls.

Of the 86 autopsy cases in this study, males outnumbered females with a male:female ratio of 1.9:1. The age range was between 33 and 90 years, with a mean age of 54.4 years.

Gupte et al. studied liver biopsies of 32 patients of Type 2 DM for features of NASH. They found that male:female ratio was 3:1 in the group showing only steatosis while it was 1:1.33 in the NASH group. Amarapurkar et al. carried out a study with 36 patients of NASH associated with diabetes showing age range of 25-75 years (mean - 50.8 years) and male:female ratio of 1.1:1.

Of the histological features studied, significant steatosis (>5%) was seen in 34 (39.5%) cases as against 8 (14.5%) controls. Most of it was macrovesicular with a variable admixture of microvesicular steatosis. Of these, majority showed Grade 1 steatosis closely followed by Grades 2 and 3. Of 100 patients of Type 2 DM studied by Gupte et al., 49% showed steatosis on ultrasonography and histology. Vasdev et al. found that the three grades of steatosis were seen in an equal proportion of patients with NAFLD.

Brunt et al. suggested necroinflammatory grading of steatohepatitis into mild, moderate, and severe on the basis of the degree of steatosis, lobular/intra-acinar, and portal inflammation along with hepatocellular ballooning. In the present study, lobular inflammation was seen in 74.4% of the cases as against 20% of the controls ($P < 0.0001$). Of these, majority showed Grade 1 ($<2$ foci/$\times 20$ field) inflammation followed by Grade 2 and Grade 3. Grade 1 (>minimal) portal inflammation was seen in 62.7% of the cases. Portal inflammation was also seen in 20% of the controls, but was mainly Grade 0 (none to minimal). This feature was also found to be significantly more common among the cases ($P < 0.0001$).

Evidence of hepatocyte injury in the form of ballooning degeneration was found in 45.3% of the cases as compared to only 5.4% of the controls. Vasdev et al. found evidence of hepatocyte injury in 53.1% of the cases of NAFLD and also in 50% of the cases of chronic hepatitis B and C. Thus, ballooning degeneration, although not specific, along with steatosis and lobular inflammation forms a common set of minimal criteria for the diagnosis of NASH.

Glycogen in the nuclei of human hepatocytes is commonly seen in DM and also in von Gierke's disease, arteriosclerosis, neoplasms, and acute suppurative inflammations. Caramia et al. demonstrated various types of nuclear glycogen deposits on electron microscopy in liver biopsies from diabetic patients. In the present study, glycogenated nuclei were seen in 68.6% of the cases as against none in controls. Hence, along with other features of NASH, the presence of glycogenated nuclei suggests the presence of diabetic changes in the liver.

Diabetes, due to the persistence of underlying insulin resistance and abnormalities of fatty acid oxidation, is a known risk factor for the progression of NASH. Fibrosis eventually results due to an increase in the connective tissue and architectural remodeling. At the time of initial presentation, 30-40% of the patients with NASH have advanced fibrosis while 10-15% of the patients have established cirrhosis. In this study, fibrosis was seen in 39.5% of the cases. Majority of these were stage 2 (portal and periportal) and 14 (16.2%) cases showed stage 3 (bridging) and stage 4 (cirrhosis) fibrosis. Vasdev et al. found fibrosis in 34.4% of the cases of NAFLD. Gupte et al. found fibrosis in 21% of the diabetics and higher degrees of fibrosis in 9.3% of the cases. In their study, they also found that longer duration of diabetes and co-existent risk factors such as obesity potentiate the progression of NASH toward higher degrees of fibrosis. It has been suggested that the presence of pericellular and perivenular fibrosis would point toward advanced disease and the potential for progression. However, this feature was not identified in any additional cases in this study even on Masson’s trichrome staining.

A curious feature noted in this study was that of the 14 cases showing stage 3 and 4 fibrosis, majority showed only mild-to-moderate degree of steatosis and lobular inflammation. This finding reiterates the fact that liver histology loses the characteristic markers of the disease as NASH progresses, ending in cirrhosis without specific etiologic features (i.e., cryptogenic cirrhosis). This has been highlighted by Poonawala et al. who found that the prevalence of type 2 diabetes was significantly higher in patients with cryptogenic cirrhosis as compared to controls.

To conclude, steatosis, lobular inflammation, portal inflammation, nuclear glycogenation, and fibrosis are the characteristic histopathological changes seen in the liver due to DM. Although these features have been demonstrated in...
liver biopsies from electively studied diabetic patients, this study highlights the histopathology of liver in autopsy cases of DM with no ante-mortem evidence of liver disease. In addition, the occurrence of fibrosis was found to be independent of the degree of steatohepatitis in cases of Type 2 DM.

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Evaluation of Knee Cartilage Defects with an Add Up Sequence of Three-dimensional Spoiled Gradient-recalled Echo Fat-saturated to Routine Magnetic Resonance Imaging of Knee

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Abstract

Introduction: Hyaline cartilage defects are one of the causes of knee pain because they may produce symptoms confused with meniscal tears. Articular cartilage pathology may be due to degenerative changes or acute injury. Conventional radiography can be used to identify gross loss of cartilage, evident as narrowing of the space in the joint, but it does not image cartilage directly. Only arthrography or combined study of arthrography with conventional radiography and computed tomography are mildly invasive and provides information limited to the contour of the cartilage surface. Magnetic resonance imaging (MRI) is the best imaging technique presently available for the evaluation of articular cartilage.

Materials and Methods: A retrospective analysis of the patients with the history of knee injury, knee pain, and features suggestive of osteoarthritis referred to MRI knee has been taken for the study. An informed consent will be obtained from the patients before any study related procedure. Patients will be imaged in GE Signa 1.5 HDxt MRI modality equipped with transmit-receive knee coil with the routine MRI knee protocol and with an extra sequence of three-dimensional (3D) spoiled gradient-recalled echo (SPGR) fat-saturated (FS). The results obtained were subjected for radiological interpretation.

Results: In all the patients who were evaluated in our study with both routine MRI knee sequences and 3D SPGR FS sequence statistically, the visibility of the evaluated structures and major cartilage pathology was excellent for routine MRI sequences and 3D SPGR FS, respectively. However, 3D SPGR FS has the sensitivity to diagnose degeneration changes and other major cartilage pathology of knee when compared to routine MRI sequences (75-85% vs. 29-38%, P < 0.001 for each comparison).

Conclusion: The additional FS 3D spoiled gradient echo sequence gives better diagnostic information of cartilage defects of knee when compared to routine MR imaging protocol of knee.

Key words: Degenerative changes, Fat-suppressed spoiled gradient-recalled echo, Hyaline cartilage, Magnetic resonance imaging, Three dimensional imaging

INTRODUCTION

Hyaline cartilage defects are one of the causes of knee pain because they may produce symptoms confused with meniscal tears. Articular cartilage pathology may be due to degenerative changes or acute injury. Osteoarthritis is an important cause in our society and is marked by degeneration of articular cartilage.
Many imaging methods are available to evaluate articular cartilage. Conventional radiography can be used to identify gross loss of cartilage, evident as narrowing of the space in the joint, but it does not image cartilage directly. Secondary changes like osteophyte formation can be seen, but the conventional radiography is not sensitive to early chondral damage detection. Only arthrography or combined study of arthrography with conventional radiography and computed tomography are mildly invasive and provides information limited to the contour of the cartilage surface.

Magnetic resonance imaging (MRI) has excellent soft-tissue contrast, so it is the best imaging technique presently available for the evaluation of articular cartilage. Recent advances in the treatment of hyaline cartilage disease have coincided with technological advances in MRI. Acute injury to cartilage can be identified using MRI. Whether the results are from degeneration or injury, MRI offers a non-invasive method of assessing the degree of damage to cartilage imaging regions of cartilage damage has the potential to provide morphologic information, like fissuring and the presence of partial- or full-thickness cartilage defects. MRI has the possibility to provide the biochemical and physiologic information about the cartilage.

Standard MRI pulse sequences used routinely for the detection of meniscal and ligamentous injuries are not adequate for assessing hyaline cartilage defects. MRI for hyaline cartilage defects with fat-suppressed (FS) spoiled gradient-recalled echo (SPGR) show hyaline cartilage with positive contrast (higher signal intensity) relative to adjacent structures.

**MATERIALS AND METHODS**

MRI images of 44 patients with the age group of 18-65 years from January 2016 to May 2016 (retrospective analysis) with clinical suspicion of osteoarthritis and with the history of knee injuries from Chettinad Hospital and Research Institute were included in the study. An informed consent will be obtained from the participating subjects. Patients referred to MRI knee were imaged in GE Signa 1.5 HDxt scanner with the routine knee protocol (proton-density [PD]-weighted sagittal and axial series, T2-weighted sagittal and coronal series, and T1-weighted coronal series) and with an add up sequence of three-dimensional (3D) SPGR for the evaluation of the knee cartilage. MR routine protocol images and 3D SPGR images of knee cartilage were assessed for focal lesions. The images obtained were subjected to radiological analysis and interpretation.

**Sample Selection**

*Inclusion criteria*
- Patients suffering from knee pain
- Patients with the history of knee injury.

*Exclusion criteria*
- Patients with any H/O metallic implants
- Patients with known cardiac pacemaker
- Pregnant women
- Claustrophobic patients.

**Image Acquisition and Image Processing**

All our patients were imaged on 1.5 Tesla GE Signa HDxt scanner. An eight channel knee coil was used. The data obtained were examined by the two radiologists independently for qualitative analysis.

**RESULT**

We had included 44 patients for this research after getting informed consent. Out of 44 patients, 3D SPGR FS sequence identified cartilage defects in 12-14 patients. Hence, routine sequences of knee in MRI with an add up sequence 3D SPGR FS sequence is better for detection of major cartilage defects in knee (Figure 1).

A patient of age 29 years old male came with the complaints of a knee injury, and the patient was referred for the MRI knee. First, the patient was screened with the routine sequences of MRI knee PD FS, T1-weighted image, T2-weighted image and then the additional sequence 3D SPGR FS was added.

The image shows chronic near complete tear noted in the anterior cruciate ligament near its femoral insertion site. Severe reduction of tibiofemoral joint space noted with near complete loss of chondral cartilage. Fraying of chondral surface noted in medial patellar facet (Figure 2).

![Image 1: Radiologist comparison between two sequences](image-url)
Ahmed, et al.: Knee Cartilage Defects

and signs are related with such defects can be confused clinically with the meniscal tears. Meniscal tears were easily cured but the treating chondral defects are difficult and of limited prediction value, because hyaline cartilage does not regenerate rather repairs within growth of fibrocartilage from subchondral mesenchyme. Increasing numbers of these studies explained the common incidence of hyaline cartilage injuries, their mimicking of cartilage pathology with meniscal tears, and clinicians lack of ability to recognize the hyaline cartilage injuries with the routine MRI techniques.

The sensitivity for assessing the lesions of the patella which was usually injured articular surface, the sensitivity was low for routine MRI protocol (21-31%), but the sensitivity is high for the 3D SPGR FS sequence (87-100%). other investigations using routine MRI pulse sequences were unable to assess Grade 1 and 2 lesions of articular cartilage. However, our data showed that such lesions of hyaline cartilage could be assessed using the 3D SPGR FS sequence.

CONCLUSION

The additional FS 3D SPGR sequence gives better diagnostic information of major cartilage defects of the knee when compared to routine MRI protocol of knee.

DISCUSSION

This study revealed that articular cartilage defects of the knee could be accurately identified on 3D SPGR FS imaging. FS 3D SPGR imaging increased the sensitivity for the identification of the articular cartilage abnormalities over routine MR protocol. Identifying hyaline cartilage defects in the knee is important because symptoms...
Comparison of Transdermal Diclofenac Patch with Intramuscular Diclofenac Injection as an Analgesic Modality Following Surgical Extraction of Impacted Mandibular Third Molars: A Cross Over Efficacy Trail

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1Professor and Head, Department of Dental Surgery, KAPV Government Medical College, Tiruchirappalli, Tamil Nadu, India, 2Assistant Professor, Department of Dental Surgery, KAPV Government Medical College, Tiruchirappalli, Tamil Nadu, India, 3Senior Intern, Department of Dental Surgery, KAPV Government Medical College, Tiruchirappalli, Tamil Nadu, India

Abstract

Introduction: The surgical removal of mandibular third molars serves as a standard model for any research pertinent to analgesia. The present study aims to analyze the effectiveness of the non-steroidal anti-inflammatory drugs, diclofenac administered by the transdermal drug delivery route as compared to intramuscular (IM) injection, in the management of post-operative pain for the standard model of surgical removal of mandibular third molars.

Materials and Methods: About 20 patients requiring bilateral mesioangular impacted mandibular third molars were selected for the study. After performing impaction surgery on right side, patients received 50-cm² patch, 100 mg of diclofenac diethylamine, and after 3 weeks surgical extraction on the left side was performed and postoperatively patients received injection diclofenac. The subjects were asked to report the intensity and pain relief on the verbal pain score chart for the 3 post-operative days.

Results: Diclofenac administered by either mode of delivery as transdermal patches or IM injections has similar effectiveness. The patients who had taken transdermal drug delivery had shown better compliance and also were enthusiastic of the prospect of achieving pain control without the need for oral medications.

Conclusion: The transdermal diclofenac patch is a promising analgesic modality for the management of mild to moderate pain following dental extractions, given the evidence of its established analgesic potency with a lower incidence of systemic adverse effects.

Key words: Diclofenac patch, Impaction surgery, Intramuscular diclofenac injection, Pain relief

INTRODUCTION

The contribution of non-steroidal anti-inflammatory drugs (NSAIDs) in the alleviation of pain cannot be underestimated. Right from the commonly used acetaminophen that affords relief by its antipyretic and analgesic effects in our day to day lives to diclofenac also commonly used for acute and musculoskeletal pain, the role of these drugs is indispensable. Though many adverse effects are commonly associated with the use of NSAIDs, these tools have to be applied at the right time with the right method to sculpt a pain free and comfortable experience for the patient.

It has been documented that the most common adverse effect with the use of NSAIDs by either oral or parenteral route is the gastric irritability that occurs secondary to the...
inhibition of the protective effects of cyclooxygenase \(^1\)\(^2\). The introduction of the transdermal drug delivery system gives a solution to the question of achieving a therapeutic concentration without producing undesirable side effects. This route of administration differs from the traditional topical administration in that, after penetration of the skin barrier, the drug enters the circulation to be distributed systemically.\(^3\) The major advantage of transdermal route is the constant drug dosage that is available and maintained in the circulation due to its sustained release properties.\(^4\)\(^5\) Thus a stable concentration is maintained systemically without concentrated higher doses in the gastrointestinal system, the hepatic metabolism is also bypassed.\(^6\)

The surgical removal of mandibular third molars serves as a standard model for any research pertinent to analgesia.\(^7\) This is due the fact that surgical removal of third molars cause pain due to both incisional and inflammatory injury, thus eliciting both peripheral and central response. Also, with the surgical removal of mandibular third molars, standardization is possible to reduce the bias caused by the level of surgical difficulty.

The present study aims to analyze the effectiveness of the NSAID, diclofenac administered by the transdermal drug delivery route as compared to intramuscular (IM) injection, in the management of post-operative pain for the standard model of surgical removal of mandibular third molars.

**MATERIALS AND METHODS**

The study was conducted among the patients reporting at the outpatient Department of Dental Surgery, Mahatma Gandhi Memorial Government Hospital attached to KAPV Government Medical College, Tiruchirappalli.

The sample included patients of the age group of 18-30 years of both sexes who were willing for the study, with bilateral mandibular third molar impactions, Winter's classification of Class I, mesioangular in position A (Figure 1). Patients with any systemic illnesses, those under chronic steroid therapy and those with a history of peptic ulceration or known allergy to NSAIDs were excluded from the study. Accordingly, 20 patients were included in this randomized controlled study. The ethical clearance for the study was provided by an institutionally approved Ethical Committee and all subjects were informed about the nature of the study and the probable side effects from the drugs being administered. A written informed consent was obtained from all subjects. The patients were divided into Group A and Group B. Group A included patients under analgesia provided by Transdermal patch, Group B included patients under analgesia provided by IM diclofenac.
diclofenac diethylamine. The matrix controlled diclofenac transdermal delivery system that provides continuous and systemic release of diclofenac and is designed to remain at the site of application for 24 h. Each 50 cm^2 patch contains 100 mg of diclofenac diethylamine as its active ingredient (Figure 4). The device consists of a polymer matrix that controls the release of the drug and an impermeable backing membrane that prevents the leaching of drug from the top. Adhesives fasten the device to the skin during use. The patch delivers a slow release of drug into the body over time, resulting in long-term effectiveness and added convenience. On the each of the following 2 days, the patch was changed and a new one placed; thus placing a total of three patches over the 3 post-operative days. Each successive application of the transdermal patch was made on a different hairless skin area (Figure 5). Paracetamol 500 mg tablets were permitted to be used as rescue medication and a total of nine tablets were provided to each of the patients for the 3 post-operative days. Surgical extraction on the left side was performed after 3 weeks and postoperatively patients received injection diclofenac (Voveron-Novartis India, 25 mg of diclofenac). Routine antibiotics were administered at the completion of the procedure. Paracetamol 500 mg tablets were permitted to be used as rescue medication and a total of nine tablets were provided to each of the patients for the 3 post-operative days. The patients were asked to maintain a record of the number of paracetamol tablets consumed on the pain assessment charts and to return the remaining tablets to operator on their next visit.

The subjects were asked to report the intensity and pain relief on the verbal pain score chart for the 3 post-operative days (Tables 1 and 2). The rescue medication tablets taken, if any, were noted, and the patients were asked if they experienced any adverse effects such as gastric discomfort, nausea, vomiting, gastric acidity or burning sensation and dyspepsia, diarrhea, dizziness, and pruritis (Table 3). Accordingly, group statistics for the parameters pain relief and duration of action (Table 4) were individually analyzed and evaluated using the Mann–Whitney U test. Statistical significance was considered for a P < 0.05 level.

RESULTS

Pain Relief
The verbal rating scale and pain relief scale were used to analyze the post-operative pain relief. The readings were done at the 2nd, 4th, 8th, 12th, and 24 h following the completion of the surgery. On the 2nd and 3rd post-operative days, the study medications were administered at a

<table>
<thead>
<tr>
<th>Table 1: Pain relief scale</th>
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<tbody>
<tr>
<td>Pain score</td>
</tr>
<tr>
<td>0</td>
</tr>
<tr>
<td>1</td>
</tr>
<tr>
<td>2</td>
</tr>
<tr>
<td>3</td>
</tr>
<tr>
<td>4</td>
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</table>

IM: Intramuscular

<table>
<thead>
<tr>
<th>Table 2: Pain intensity scale</th>
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</thead>
<tbody>
<tr>
<td>Pain score</td>
</tr>
<tr>
<td>0</td>
</tr>
<tr>
<td>1</td>
</tr>
<tr>
<td>2</td>
</tr>
<tr>
<td>3</td>
</tr>
<tr>
<td>4</td>
</tr>
</tbody>
</table>

IM: Intramuscular
particular reference time and the readings done accordingly. As per the results given in Table 4, the mean pain relief at 1st day was 0.41 for Group A with a standard deviation (SD) of 0.840 and 0.64 for Group B with a SD of 1.059. The Mann–Whitney test was 112 and the significance from two-tailed t-test was 0.707 for both the groups. The mean pain relief at 2nd day was 1.24 for Group A with a SD of 1.149 and the mean pain relief for Group B was 1 with a SD of 1.149. The Mann–Whitney test was 91.00 with the significance by two-tailed t-test being 0.350 for both the groups. The mean pain relief at 3rd day was 1.40 for Group A with a SD of 0.887 and 1.00 for Group B with a SD of 0.944. The value from Mann–Whitney test was 112.00 and the significance calculated from two-tailed t-test was 0.847. Thus the results for post-operative pain relief were not statistically significant which as represented in Table 5 and Graph 1 showed similar level of efficacy by both patches and drugs.

**Duration of Action**

About 6 patients took oral medication (paracetamol tablet) at 4 h after application of patch, while 13 patients took tablets after 8 h. Only one patient took oral medication after 3 h, this could be probably due to the level of anxiety associated to the procedure. Group A had a mean duration of action of 5.070 with a SD of 1.6870, the significance of this finding by two-tailed t-test was 0.475. Group B had a mean duration of action for 4.586 with a SD of 1.9368, and significance form two-tailed t-test was 0.475. Thus, as per the representation shown in Table 6, both the groups had no statistically significant differences in terms of duration of action with Group A showing a slightly higher value than Group B which was not statistically significant.

### Pain Intensity

An assessment of the intensity of pain following mandibular third molar extractions revealed that there was a gradual decrease in the pain intensity scores from day 1 to day 3 with both IM injection as well as transdermal patch (Table 7 and Graph 2). Statistical analysis using the Mann–Whitney U test however reveals that the difference in the pain intensity as well as in the pain relief provided by IM injection and transdermal patch was not statistically significant (Table 8).

<table>
<thead>
<tr>
<th>Table 3: Discomforts experienced</th>
</tr>
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<tbody>
<tr>
<td>None</td>
</tr>
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<table>
<thead>
<tr>
<th>Table 4: Onset of pain: Duration of action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time of drug intake/application</td>
</tr>
<tr>
<td>1st h</td>
</tr>
<tr>
<td>Pain onset</td>
</tr>
<tr>
<td>Duration of action</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Table 5: Post-operative pain relief</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group</td>
</tr>
<tr>
<td>-------</td>
</tr>
<tr>
<td>Pain relief at 1st day</td>
</tr>
<tr>
<td>Group A</td>
</tr>
<tr>
<td>Group B</td>
</tr>
<tr>
<td>Pain relief at 2nd day</td>
</tr>
<tr>
<td>Group A</td>
</tr>
<tr>
<td>Group B</td>
</tr>
<tr>
<td>Pain relief at 3rd day</td>
</tr>
<tr>
<td>Group A</td>
</tr>
<tr>
<td>Group B</td>
</tr>
</tbody>
</table>

<table>
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<tr>
<th>Table 6: Duration of action</th>
</tr>
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<tbody>
<tr>
<td>Group</td>
</tr>
<tr>
<td>-------</td>
</tr>
<tr>
<td>Duration of action (h)</td>
</tr>
<tr>
<td>Group A</td>
</tr>
<tr>
<td>Group B</td>
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</tbody>
</table>
Table 7: Score on the pain intensity scale

<table>
<thead>
<tr>
<th></th>
<th>Intramuscular</th>
<th></th>
<th>Transdermal system</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Day 1</td>
<td>Day 2</td>
<td>Day 3</td>
<td>Day 1</td>
</tr>
<tr>
<td>Mean (n=20)</td>
<td>1.1100</td>
<td>0.6100</td>
<td>0.3433</td>
<td>1.2767</td>
</tr>
<tr>
<td>SD</td>
<td>0.0139</td>
<td>0.6847</td>
<td>0.5567</td>
<td>0.7497</td>
</tr>
</tbody>
</table>

SD: Standard deviation

Table 8: Showing the Mann–Whitney U test values for pain intensity and pain relief when comparing intramuscular and transdermal diclofenac formulations

<table>
<thead>
<tr>
<th></th>
<th>Day 1</th>
<th>Day 2</th>
<th>Day 3</th>
<th>Day 1</th>
<th>Day 2</th>
<th>Day 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mann–Whitney U</td>
<td>0.1000</td>
<td>1.2297</td>
<td>1.0819</td>
<td>0.8433</td>
<td>0.1770</td>
<td>0.0139</td>
</tr>
<tr>
<td>P value</td>
<td>0.328</td>
<td>0.233</td>
<td>0.294</td>
<td>0.280</td>
<td>0.420</td>
<td>0.260</td>
</tr>
</tbody>
</table>

DISCUSSION

NSAIDs have the ability to reduce both pain and inflammation as a result they, are the ideal analgesic agents for the control of pain in the event of surgical removal of mandibular third molar impactions. Surgical tooth removal causes a typical type of pain which reaches peak values in the immediate extraction period and thereafter reaches moderate levels. In that respect for the procedure of surgical removal of mandibular third molars, anesthesia during the procedure is important; however, adequate pain control is also important in the immediate post-operative period as the pain from surgical removal of third molar reaches its peak level in the immediate post-operative period. In this study, we had standardized the level of difficulty of the procedure, operator variability, and patient inclusion and exclusion criteria.

The results of our study show that the pain relief at 1st, 2nd, and 3rd day for patches is seen by the pain scores of 0.41, 1.24, and 1.40, respectively, whereas for IM diclofenac, the values are 0.64, 1.00, and 1.00. Though these two ranges of values show no statistically significant difference and are not statistically significant, the mild variations between these values show that in the 4th h when the action of local anesthetic is completely reversed, diclofenac injection have shown better pain management, probably due to the sufficient plasma levels available to combat the post-operative pain. However, at the 6th h, patches appear to show better pain control probably because they had achieved a more constant therapeutically effective concentration by this time comparable to injectable form.

These results observed in our study are similar to the results seen in the studies done by Bhaskar et al., Bachalli et al., and Krishna. In the study by Bhaskar et al., IM
Selvi, et al.: Efficacy of Transdermal Diclofenac Patch

Table 9: Efficacy of the treatment

<table>
<thead>
<tr>
<th></th>
<th>Effective</th>
<th>Not effective</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Injection</td>
<td>10</td>
<td>10</td>
<td>20</td>
</tr>
<tr>
<td>Patch</td>
<td>13</td>
<td>7</td>
<td>20</td>
</tr>
<tr>
<td>Total</td>
<td>23</td>
<td>17</td>
<td>40</td>
</tr>
</tbody>
</table>

Injection event rate=51.00%, patch event rate=67.00%, injection event odds=100.00%, patch event odds=185.71%

Graph 3: Distribution of patients reporting significant pain relief from day 1 to day 3

Diclofenac had shown better pain management in the first post-operative day compared to transdermal diclofenac patches for patients undergoing therapeutic extraction of premolars. The results also showed that while 51% of the subjects on IM diclofenac showed a pain relief on the 2nd post-operative day, 67% of the patients on transdermal patches showed pain relief on the 2nd post-operative day. However, there was a complete pain relief in both the groups on the 3rd post-operative day. Similar results were also observed in a study by Bachalli et al., it was seen that the pain relief at 2 h was significantly better with administration of IM diclofenac compared to transdermal patches in patients undergoing surgical removal of impacted mandibular third molar. There was no statistically significant difference between either routes of administration in the pain relief score on the measurement taken subsequently for 3 consecutive days. There was also difference in the pain level of the patients when they had opted for an analgesic. While some patients had taken an analgesic when only little pain had been experienced, others waited for a higher intensity of pain before they had taken the analgesic. The results for two forms of diclofenac had been similar in another study by Krishna, where 100 mg of transdermal patches had been administered at start of the surgery and 75 mg of IM diclofenac was given half an hour before the completion of the procedure in patients undergoing orthopedic limb surgery, there was no statistically significant difference in the visual analog scale between the two groups at 2 h. However, at 6 h, 15 patients in the transdermal group and 13 patients in the oral group showed a pain intensity score of 2. The results of this study had shown that both transdermal diclofenac and IM diclofenac had shown similar pain relief. In a similar study by Krishna comparing transdermal diclofenac and IM diclofenac for orthopedic limb surgery, the duration of action for transdermal patches had been for 8 h and 6 min and for IM diclofenac had been for 7 h and 28 min.

In the study by Bhaskar et al., they also concluded in his study that diclofenac transdermal patches were well tolerated by the patients, 2 patients had reported gastric irritation and nausea following the intake of oral diclofenac tablets. In a meta analyses by Mason et al., it has been shown that topical NSAIDs do not show any serious gastrointestinal injury or increased chances of renal failure. Also in a study by Naesdal et al., it has been shown that the overall gastrointestinal complications such as ulcer and dyspepsia were statistically significantly lower with the use of topical NSAIDs due to their lower systemic concentrations. Apart from the discomforts, the patients who had taken transdermal drug delivery had shown better compliance and also were enthusiastic of the prospect of achieving pain control without the need for oral medications, as was previously experienced in the study by Bhaskar et al.

CONCLUSION

The transdermal diclofenac patch seems to be a promising analgesic modality for the management of mild to moderate pain following dental extractions, given the evidence of its established analgesic potency with a lower incidence of systemic adverse effects. Transdermal diclofenac therapy may have a role to play in post-traumatic pain, perhaps with an increased strength of the analgesic drug in the transdermal patch. However, longer clinical trials with a larger sample need to be conducted before the real scope of the transdermal diclofenac patch for surgical dental extractions can be clearly defined.

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Selvi, et al.: Efficacy of Transdermal Diclofenac Patch


Source of Support: Nil, Conflict of Interest: None declared.
Correlation of Bone Marrow Iron Storage with Different Types of Anemia

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Nutritional anemia, particularly iron deficiency, continues to be a major public health problem worldwide, particularly in the developing nations. A combination of surrogate markers, namely serum ferritin, serum iron, total iron binding capacity, and percentage saturation of transferrin are routinely employed to assess the iron status of an individual.

Materials and Methods: It was a cross-sectional study conducted in the Department of Pathology, Rajendra Institute of Medical Sciences (RIMS), Ranchi. Air dried smears prepared from a total of 50 subjects referred to the Pathology Department for investigation, the peripheral blood and bone marrow from different patients obtained from the Pathology Department of RIMS.

Results: About 24% cases had ferritin <14 ng/ml with the bone marrow iron stores Grade 0-2. 12% had ferritin 15-25 ng/ml with bone marrow iron store between Grades 0 and 2. About 6% of cases had ferritin between 45 and 100 ng/ml with bone marrow iron stores between Grades 2 and 4. Nearly 8% of cases had ferritin between 100 and 200 ng/dl with bone marrow iron store between Grades 1 and 3. 18% cases had ferritin between 200 and 500 ng/ml with bone marrow iron stores between Grades 1 and 3. 20% of cases had ferritin 500-2000 ng/ml with bone marrow iron stores between Grade 2 and 4. 20% cases had ferritin >2000 ng/ml with bone marrow iron stores Grade 3-4.

Conclusion: Microscopic examination of stainable iron in bone marrow is a reliable technique in assessing iron stores. In the present study, it has been found that all cases of iron deficiency anemia had low iron stores. Serum ferritin value when <14 ng/dl is diagnostic of iron deficiency anemia while raised serum ferritin does not exclude iron deficiency anemia. Serum iron correlates well with the bone marrow iron stores level.

Key words: Anemia, Bone marrow, Gales criteria, Perls staining

INTRODUCTION

According to the World Health Organization, anemia is defined as a condition in which the hemoglobin content is below normal. This situation occurs because of different patho-physiological mechanisms. The most prevalent types of anemia are due to nutritional deficiencies (malnutrition and iron, vitamin B12, and folic acid deficiencies) and chronic diseases (such as cancer, kidney disease, and congestive heart failure).¹²

Nutritional anemia, particularly iron deficiency, continues to be a major public health problem worldwide, particularly in the developing nations.³ A combination of surrogate markers, namely serum ferritin, serum iron, total iron binding capacity, and percentage saturation of transferrin are routinely employed to assess the iron status of an individual.⁴⁶

Anemia is a major health problem in India. In the 2005-2006 National Family Health Survey (NFHS-3), a household survey aimed at having national and state representative data on population health and nutrition; the prevalence of anemia was 70% in children aged 6-59 months, 55% in females aged 15-49 years, and 24% in males aged 15-49 years.⁷ Although the NFHS-3 showed that the prevalence of anemia was higher in rural areas, there is a paucity of data about the epidemiology of anemia in rural settings.⁸
In order to characterize the type of anemia and formulate a differential diagnosis, the work-up should include physical exams and laboratory tests, such as evaluations of hematocrit, hemoglobin, and red blood cell (RBC) indices. The RBC indices should include the cell count, mean cell volume, mean corpuscular hemoglobin (MCH), MCH concentration (MCHC), and red cell distribution width (RDW).³

**MATERIALS AND METHODS**

It was a cross-sectional study conducted in the Department of Pathology, Rajendra Institute of Medical Sciences (RIMS), Ranchi. Air-dried smears prepared from a total of 50 subjects referred to the Pathology Department for investigation, the peripheral blood, and bone marrow from different patients obtained from Pathology Department of RIMS.

Both peripheral blood and bone marrow smears were stained by Leishman stain to diagnose the type of anemia. The cases diagnosed as anemia were included in the study and bone marrow iron staining along with serum ferritin levels was performed. Iron staining of the bone marrow smears was done by Perl's method.⁴

In all cases of anemia the following routine investigation were done: Hemoglobin estimation, total RBC count, white blood cell count, differential count, hematocrit, mean corpuscular volume, MCH, MCHC, platelet count, Red cell distribution width - standard deviation (RDW-SD), Red cell distribution width - coefficient of variation (RDW-CV).

Bone marrow aspirate was obtained after informed consent from the posterior iliac spine and ant. Iliac spine observing strict asepsis, spread on to a slide; air-dried, fixed with methanol at the same setting for hemoglobin and serum ferritin level estimation. Grading was done according to Gale’s method of bone marrow iron grading.⁵

**Procedure**

In the first step, sample and anti-ferritin coated paramagnetic micro-particles are combined. Ferritin present in the sample binds to anti-ferritin coated paramagnetic micro particles. After washing anti-ferritin, acridinium coated labeled conjugate to add in the second step. Pretrigger and trigger solution are then added to the reaction mixture, the resulting chemiluminescent reaction is measured in relative light units. A direct relationship exists between the amount of ferritin in the sample and relative light units detected by the architect optical system.

**Data Analysis**

Data were entered and analyzed using Microsoft Excel 2007.

**RESULTS**

The Table 1 shows the relative frequency of different types of anemia in present study. Among all the anemia, iron deficiency anemia was the most common anemia constituting of 40% of cases followed by anemia of chronic disease 26%; aplastic anemia 16%; others 6%, megaloblastic anemia 6%; hemolytic anemia 6%.

The Table 2 shows age wise distribution of different types of anemia; 12% of cases were between 1 and 10 years. 32% of cases were between 10 and 20 years of age. About 40% of cases were between 20 and 40 years; 12% cases were between 40 and 60 year of age; and 4% of cases were above 60 years.

The Table 3 shows sex wise distribution of different types of anemia. About 12% of males were affected from iron deficiency anemia, while 28% of female were affected from iron deficiency anemia. About 12% males were affected from anemia of chronic disease while 14% of female were affected from anemia of chronic disease. About 10% of males were affected from aplastic anemia, while 6% males were affected from aplastic anemia. Around 6% of males were affected from megaloblastic anemia 2% of females were affected from hemolytic anemia, while 4% of males were affected from hemolytic anemia. About 4% of females were affected from others (anemia of leukemia, Myelodysplastic syndrome [MDS]), while 4% of males were affected from others (anemia of leukemia, MDS).

The Table 4 shows the correlation of serum ferritin with bone marrow iron stores. About 24% cases had ferritin <14 ng/ml with the bone marrow iron stores Grade 0-2. About 12% had ferritin 15-25 ng/ml with bone marrow iron store between Grades 0 and 2. About 6% of cases had ferritin between 45 and 100 ng/ml with bone marrow iron stores between Grades 2 and 4. About 8% of cases had ferritin between 100 and 200 ng/ml with bone marrow iron store between Grades 1 and 3. About 18% cases had ferritin between 200 and 500 ng/ml with bone marrow iron stores.

<table>
<thead>
<tr>
<th>Types of anemia</th>
<th>Number of cases</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Iron deficiency anemia</td>
<td>20</td>
<td>40</td>
</tr>
<tr>
<td>Aplastic anemia</td>
<td>8</td>
<td>16</td>
</tr>
<tr>
<td>Anemia of chronic disease</td>
<td>13</td>
<td>26</td>
</tr>
<tr>
<td>Hemolytic anemia</td>
<td>3</td>
<td>6</td>
</tr>
<tr>
<td>Megaloblastic anemia</td>
<td>3</td>
<td>6</td>
</tr>
<tr>
<td>Others (associated with leukemia, MDS etc.)</td>
<td>3</td>
<td>6</td>
</tr>
<tr>
<td>Total</td>
<td>50</td>
<td>100</td>
</tr>
</tbody>
</table>

MDS: Myelodysplastic syndrome

---

**Table 1: Relative frequency of different types of anemia**

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Tabassum, et al.: Bone Marrow Iron Storage In different types of Anemia
Iron stores between Grades 1 and 3. About 20% of cases had ferritin 500-2000 ng/ml with bone marrow iron stores between Grade 2 and Grade 4. About 20% cases had ferritin >2000 ng/ml with bone marrow iron stores Grade 3-4.

**DISCUSSION**

In the present study, the majority of cases were from 20 to 40 years (42%) of age group. Next group was 10-20 years (28%) of age group. Iron deficiency anemia was more common in females and anemia of chronic disease was more common in males. Similar findings were observed in a study conducted by Pujara et al. in 2014.12

**Predominant Marrow Findings in Different Types of Anemia**

In the present study, predominant bone marrow finding in iron deficiency anemia was mild to moderate normoblastic erythroid hyperplasia with bone marrow iron stores of Grade 0-2, which correlated with study done by Pujara et al. and Bableshwar et al.12,13

In the present study, 16% cases had serum ferritin <14 ng/ml with bone marrow iron stores from Grade 0-2. About 12% cases had ferritin 15-25 ng/ml with bone marrow iron stores between Grades 0 and 2. About 6% cases had ferritin between 45 and 100 ng/ml with bone marrow iron stores between Grades 2 and 4. P value was <0.03 when compared with the bone marrow iron stores.

<table>
<thead>
<tr>
<th>Serum ferritin (ng/dl)</th>
<th>Number of cases</th>
<th>Bone marrow iron stores</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;14</td>
<td>12</td>
<td>Grade 0-2</td>
</tr>
<tr>
<td>15-25</td>
<td>2</td>
<td>Grade 0-2</td>
</tr>
<tr>
<td>25</td>
<td>0</td>
<td>Grade 0-2</td>
</tr>
<tr>
<td>45-100</td>
<td>3</td>
<td>Grade 2-4</td>
</tr>
<tr>
<td>100-200</td>
<td>4</td>
<td>Grade 1-3</td>
</tr>
<tr>
<td>200-500</td>
<td>9</td>
<td>Grade 1-3</td>
</tr>
<tr>
<td>500-2000</td>
<td>10</td>
<td>Grade 2-4</td>
</tr>
<tr>
<td>&gt;2000</td>
<td>10</td>
<td>Grade 3-4</td>
</tr>
</tbody>
</table>

There was also the presence of siderotic granules in erythroblasts in variable number in megaloblastic anemia. The study correlates with study of Bableshwar et al. in study of 80 patients and Krause and Stolc in a study on 104 patients.13,14

**CONCLUSION**

Microscopic examination of stainable iron in bone marrow is a reliable technique in assessing iron stores. In the present study, it has been found that all cases of iron deficiency anemia had low iron stores. Serum ferritin value when
<14 ng/dl is diagnostic of iron deficiency anemia while raised serum ferritin does not exclude iron deficiency anemia. Serum iron correlates well with the bone marrow iron stores level.

REFERENCES

A Study of Clinical Profile and Subtypes of Acute Ischemic Stroke in a Tertiary Care Center

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Abstract

Background: Stroke is a major public health problem and has high mortality and morbidity rate. There is great variability seen in clinical presentation and etiology of stroke patients. Ischemic stroke needs to be classified into subtypes, for proper treatment and prognosis.

Objective: To study the clinical pattern of stroke and to identify the risk factors in various subtypes of acute ischemic stroke according to Trial of Org 10172 in acute stroke treatment (TOAST) criteria.

Materials and Methods: This was an observational non-interventional study, where a total of 240 consecutive patients of both sex and age more than 20 years of age presenting as first-ever acute stroke were evaluated in the Department of Medicine, Chirayu Medical College and Hospital, Bhopal. Ischemic stroke patients were further classified into subtypes as per TOAST classification.

Results: In our study, 175 patients (72.9%) had ischemic stroke and 65 patients (27.1%) had hemorrhagic stroke. The mean age was 53.02 ± 14.38 years in ischemic stroke group and 52.84 ± 12.45 years in hemorrhagic stroke group. Overall stroke patients included 172 (71.67%) males and 68 (28.33%) females (M: F = 2.53:1). In ischemic stroke patients, 130 (74.28%) were males and 45 (25.71%) were females. In hemorrhagic group, 42 (64.61%) were males and 23 (35.38%) were females. Overall index stroke was on the left side in 113 (47.08%) patients, and it was on the right side in 125 (52.08%) patients. 2 (0.08%) patients also had bilateral stroke (thalamus). Almost similar proportion of laterality was seen in ischemic and hemorrhagic stroke patients. Most common risk factors were dyslipidemia (62.86%), hypertension (52.57%), smoking (41.14%), and diabetes (29.14%). As per the TOAST classification of ischemic stroke, it was observed that 72 cases (41.1%) had large vessel atherothrombotic disease, 27 cases (15.4%) had small vessel disease (lacunar infarcts), 28 cases (16%) had cardioembolic strokes, 4 cases (2.2%) had stroke due to determined etiology, and 44 cases (25.1%) had stroke of undetermined etiology.

Conclusion: Most of the patients had ischemic stroke as compared to hemorrhagic stroke. It was more common in males. Most patients had large vessel disease. The study contributes to understanding of demographic characteristics, risk factors, and stroke subtypes in acute ischemic stroke. Large vessel atherosclerosis is the most common subtype, as in other Asian studies. The importance of various risk factors among ischemic stroke subtypes should be stressed for prompt preventive strategies and treatment.

Key words: Ischemic stroke, Risk factors, TOAST criteria

INTRODUCTION

Stroke is one of the leading causes of morbidity and mortality worldwide.1 Ischemic strokes account for 50-85% of all strokes worldwide.2 Stroke case - fatality defined as the proportion of events that are fatal within 28 days post stroke averages 30%.3 Stroke is also a leading cause of disability in adults. Among the stroke survivor each year, 30% requires assistance with activities of daily living, 20% requires assistance with ambulation, and 16% requires institutional care leading to serious long-term physical and mental disabilities among survivors.4 Thus, it is apparent that stroke is a major public health problem and has high mortality and morbidity rate.

Ischemic stroke has subtypes with variable underlying pathogenesis and studies on ischemic stroke as a whole without subtype classification may inadequately evaluate risk...
factors. Thus, ischemic stroke needs proper classification into its subtypes, which helps in proper diagnosis, treatment, and research. Subtyping of stroke reduces the heterogeneity of ischemic stroke phenotype. There are very few studies on stroke subtype classification in India.

**Objective**

The aim of this study was to evaluate the clinical pattern of stroke and to identify the various risk factors in subtypes of acute ischemic stroke according to the Trial of Org 10172 in Acute Stroke Treatment (TOAST) criteria.

**MATERIALS AND METHODS**

This was an observational and non-interventional study, where a total of 240 consecutive patients of both sex and age more than 20 years presenting as first-ever acute stroke were evaluated in the Department of Medicine, Chirayu Medical College and Hospital, Bhopal. This study was done with the following inclusion and exclusion criteria:

**Inclusion Criteria**

1. Subjects aged older than 20 years
2. The diagnosis of acute stroke (ischemic/hemorrhagic) based on clinical evaluation and imaging (computed tomography [CT]-head/magnetic resonance imaging [MRI] brain).

**Exclusion Criteria**

1. Patients with stroke-like conditions due to systemic diseases such as infections and trauma
2. All hemorrhagic stroke patients who have posttraumatic, drug-induced (e.g., anticoagulant-induced), and those with bleeding diathesis-related etiologies will be excluded
3. Patients in whom the whole investigation protocol was not possible.

**Clinical Definition of Acute Stroke**

Clinically, the stroke will be defined as per the WHO definition. According to the WHO, stroke is a clinical syndrome characterized by rapidly developing clinical symptoms and/or signs of focal and at times global (applied to patients in deep coma and those with subarachnoid hemorrhage) loss of cerebral function with symptoms lasting more than 24 hrs or leading to death, with no apparent cause other than that of vascular origin.

All the patients fulfilling the definition of acute stroke were subjected to CT scan head (plain) and MRI brain involving standard sequences of T1WI, T2WI, fluid attenuation inversion recovery image, diffusion-weighted imaging with apparent diffusion coefficient and gradient echo imaging. All the patients were assessed clinically through detailed history and clinical examination. From the history, various demographic variables were collected including age, sex, history of transient ischemic attack/stroke, hypertension, diabetes mellitus, coronary artery disease, prestroke disability, smoking, and family history of stroke. Routine hematological and biochemical tests including Hb, total leukocyte count, erythrocyte sedimentation rate, blood sugar, and lipid profile were done. Electrocardiogram (ECG), echocardiography, and carotid Doppler study were done in all patients. After the availability of the results of all investigations, ischemic stroke patients were grouped according to the TOAST subtypes.

**Statistical Analysis**

All the data were fed on excel spreadsheet, and statistical analyses were made using Epi Info version 3.3.2.

**RESULTS**

**Age and Sex**

The age range of the study group was 24-88 years. The study group included 172 (71.67%) males and 68 (28.33%) females (M: F = 2.53:1). 175 patients (72.9%) had ischemic stroke and 65 patients (27.1%) had hemorrhagic stroke. The mean age was 53.02 ± 14.38 years in ischemic stroke group and 52.84 ± 12.45 years in hemorrhagic stroke group. In ischemic stroke patients, 130 (74.2%) were males and 45 (25.8%) were females. In hemorrhagic group, 42 (64.6%) were males and 23 (35.4%) were females (Tables 1 and 2).

**Age Distribution**

Overall about half (55%) of stroke patients were in the age group 41-60 years, 18.3% patients were of age ≤40 years, and 27.5% of patients were having age more than 60 years (Table 3).

**Routine Investigations**

The routine laboratory investigations revealed normal renal functions and liver functions in all the cases. ECG showed evidence of ischemia in 14 patients, left ventricular...
hypertrophy in 10 patients, and atrial fibrillation in 6 patients.

**Index Stroke Characteristics**

*Type of index stroke*

In our study, 175 patients (72.9%) had ischemic stroke and 65 patients (27.1%) had hemorrhagic stroke (Table 1).

*Laterality of index stroke*

Overall index stroke was on the left side in 113 (47.08%) patients and it was on the right side in 125 (52.08%) patients. 2 (0.08%) patients also had bilateral stroke (thalamus). Almost similar proportion of laterality was seen in ischemic and hemorrhagic stroke patients (Table 4).

**Etiological Evaluation of Ischemic Stroke**

There were 175 cases of ischemic stroke in our study. The TOAST classification was used to classify these cases based on etiology. Besides the clinical features, other investigations done to classify these cases were routine investigations such as blood sugar, lipid profile, MRI (brain), intracranial MR angiography, transthoracic echocardiography, and carotid Doppler. Only in cases in which no abnormality could be detected on these primary investigations, extensive battery of investigations was done to find out any other determined etiologies of stroke.

Thus, using TOAST classification, it was observed that 72 cases (41.1%) had large vessel atherothrombotic disease, 27 cases (15.4%) had small vessel disease (lacunar infarcts), 28 cases (16%) had cardioembolic strokes, 4 (2.2%) cases had stroke due to determined etiology, and 44 cases (25.1%) had stroke of undetermined etiology (Table 5).

**Risk Factor Assessment of Ischemic Stroke Patients**

Among ischemic stroke patients, 92 (52.57%) patients were hypertensive, 51 (29.14%) patients were diabetic, 110 (62.86%) patients had dyslipidemia, and 72 (41.14%) patients were smokers. History suggestive of coronary artery disease was present in 10 (5.71%) patients, atrial fibrillation was present in 6 (3.43%) patients, and 8 (4.57%) patients had rheumatic heart disease. 24 (13.71%) patients had history of transient ischemic attack or previous stroke (Table 6).

**DISCUSSION**

The mean age of our stroke patients was 53.02 ± 14.38 years for ischemic stroke and 52.84 ± 12.45 years for hemorrhagic stroke which was relatively younger than those seen in the Western studies. In the Indian subcontinent, stroke happens nearly a decade earlier than West and young strokes constitute about 20% of stroke population in India; at least in the clinical studies, although in some recent epidemiological studies, the overall proportion of younger stroke patients was lesser. In both ischemic and hemorrhagic stroke types, about half of the patients were in age group 41-60 years. This may probably because the demographic profile of the Indian population is having a relatively large young base and small top. Our study cohort also had a sizable number, i.e., 42 (17.5%) patients who were 40 years of age or less and 66 (27.5%) were aged more than 60 years. These figures are generally in agreement with hospital-based cohort described in Indian studies. The gender distribution showed an M:F ratio of 2.89:1 in ischemic stroke and 1.83:1 in hemorrhagic stroke patients. This gender difference possibly resulted from inherent social bias, in which female patients are less likely to be admitted to hospital compared to male patients. Our study was comparable to other Indian studies on stroke patients where greater preponderance was seen among males. In our study, 175 (72.9%) patients had ischemic stroke, whereas 65 (27.1%) patients had hemorrhagic stroke. This is consistent with the reported proportion of ischemic stroke of 68% from community-based studies to 80% from hospital-based study. We classified 175

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**Table 3: Age distribution of patients as per stroke type**

<table>
<thead>
<tr>
<th>Age range (years)</th>
<th>Ischemic</th>
<th>Hemorrhagic</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>20-40</td>
<td>32 (18.28)</td>
<td>10 (15.3)</td>
<td>42 (17.5)</td>
</tr>
<tr>
<td>41-60</td>
<td>92 (52.5)</td>
<td>40 (61.5)</td>
<td>132 (55.0)</td>
</tr>
<tr>
<td>61-80</td>
<td>49 (28.0)</td>
<td>15 (23.0)</td>
<td>64 (26.6)</td>
</tr>
<tr>
<td>&gt;80</td>
<td>2 (1.14)</td>
<td>0</td>
<td>2 (0.83)</td>
</tr>
<tr>
<td>Total</td>
<td>175 (100.0)</td>
<td>65 (100.0)</td>
<td>240 (100.0)</td>
</tr>
</tbody>
</table>

**Table 4: Laterality of index stroke**

<table>
<thead>
<tr>
<th>Laterality</th>
<th>Ischemic stroke</th>
<th>Hemorrhagic stroke</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Right</td>
<td>93 (53.1)</td>
<td>32 (49.2)</td>
<td>125 (52.08)</td>
</tr>
<tr>
<td>Left</td>
<td>80 (45.7)</td>
<td>33 (50.8)</td>
<td>113 (47.08)</td>
</tr>
<tr>
<td>Bilateral</td>
<td>02 (1.14)</td>
<td>0 (0)</td>
<td>2 (0.08)</td>
</tr>
<tr>
<td>Total</td>
<td>175 (100.0)</td>
<td>65 (100.0)</td>
<td>240 (100)</td>
</tr>
</tbody>
</table>

**Table 5: Etiology of index acute ischemic stroke by TOAST criteria**

<table>
<thead>
<tr>
<th>TOAST category</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>LV</td>
<td>72 (41.1)</td>
</tr>
<tr>
<td>SV</td>
<td>27 (15.4)</td>
</tr>
<tr>
<td>CE</td>
<td>28 (16.0)</td>
</tr>
<tr>
<td>Determined etiology</td>
<td>04 (2.2)</td>
</tr>
<tr>
<td>Undetermined</td>
<td>44 (25.1)</td>
</tr>
<tr>
<td>Total</td>
<td>175 (100.0)</td>
</tr>
</tbody>
</table>
ischemic stroke patients according to the TOAST subtypes. Maximum numbers of patients 72 cases (41.1%) had large vessel atherothrombotic disease, 27 cases (15.4%) had small vessel disease. (lacunar infarcts), 28 cases (16%) had cardioembolic strokes, 4 (2.2%) cases had stroke due to specific determined etiology, such as Takayasu’s arteritis, and 44 cases (25.1%) had stroke of undetermined etiology. Our findings were consistent with the available Indian data of ischemic stroke subtypes. A hospital-based registry of Southern India has attributed 41% of strokes to large artery atherosclerosis, 18% to lacunar causes, 10% to cardioembolic causes, 4% to specific causes, and the remaining 27% of the cases to undetermined etiology. We had a slightly greater proportion of cardioembolic strokes possibly due to the fact that our center is a tertiary care center catering various cardiac illnesses and cardiac interventions.

CONCLUSION

Incidence of stroke is on rise in our country. Most of the patients had ischemic stroke as compared to hemorrhagic stroke. The sex distribution of stroke patients showed that it was more common in males. Most patients had large vessel disease. There should be emphasis on the various risk factors of ischemic stroke subtypes for preventive strategies and treatment.

REFERENCES

Clinical Features and Microbiological Profile of Necrotizing Fasciitis at a Tertiary Care Centre

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Abstract

Introduction: Necrotizing fasciitis (NF) is a major global surgical emergency and still considered as a social disease in India reflecting the standards of living in a community.

Aim: The aim of the present study was to study microbiological profile of NF along with surgical features.

Materials and Methods: About 50 cases of NF were studied over a period of 9 months in Katihar Medical College between 2015 and 2016 with emphasis on the mode of presentation and microbiological profile.

Results: Maximum 36% of the cases were in the age group of 51-60 years. The sex incidence revealed a male to female ratio of 11.5:1 showing a male preponderance particularly affecting those who were engaged in outdoor activities such as farming. Diabetes mellitus was the most common risk factors in these patients. Streptococcus, Pseudomonas, and Escherichia coli were the most common organism isolated in wound cultures. Organisms were mostly sensitive to aminoglycosides such as amikacin, gentamicin, and fluorquinolones.

Conclusion: NF has varied presentations as shown by this study with predominant symptoms of tenderness and edema. Good results can be obtained by adopting a multidisciplinary approach along with prompt diagnosis and surgical care in hospital settings, health education, and awareness about dreaded complication of this disease.

Key words: Culture, Diabetes mellitus, Necrotizing fasciitis, Pseudomonas, Wound

INTRODUCTION

Necrotizing fasciitis (NF) is a rapidly progressing infection of the skin and soft tissues that has been known since the days of Hippocrates. Early diagnosis and surgical intervention is of utmost importance in reducing mortality and amputation rates resulting from NF as it causes extensive necrosis of the fascia and subcutaneous tissue leading to severe systemic toxicity. Its rarity and the paucity of early pathognomonic signs make NF a major diagnostic challenge. The term “Necrotizing fasciitis” was coined by Wilson in 1952, for he observed that cutaneous gangrene is not only the clinical diagnostic sign, but also fascial necrosis is a constant feature. It is usually accompanied by the systemic inflammatory response syndrome and needs prolonged intensive care treatment. The overall incidence of NF has been estimated as 0.24-0.4/100,000 adults. In South East Asian countries, it is associated with 30-70% mortality despite advancement in therapy. According to the microbiological characteristics, NF is classified as follows: Type 1 (polymicrobial) and Type 2 (monomicrobial), the former being more common. Type I NF also known as synergistic NF is a mixed infection caused by anaerobic, aerobic, and facultatively anaerobic Gram-positive and Gram-negative bacteria. Most of the pathogens originate from the bowel flora e.g., Escherichia coli, Pseudomonas spp., Bacteroides spp., and Vibrio spp. Risk factors include immune compromise, recent surgery, and underlying abdominal pathology including malignancy. Type II NF is usually monomicrobial and due to Gram-positive organisms. The most common pathogen causing Type II

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NF is Group A β-hemolytic *Streptococcus* either alone or in combination with other species, usually *Staphylococcus aureus*. Cases of NF without a recognized precipitating factor are more likely to be due to streptococcal infection or, more recently, due to community-acquired methicillin-resistant staphylococcal infection. The earliest clinical feature common to all types of NF is exquisite pain, often out of proportion to any visible skin changes. This is due to the occlusion of perforating nutrient vessels with resultant nerve infarction. Pain progresses until the nerves supplying the skin are destroyed resulting in anesthesia of the affected areas. Early clinical suspicion and surgery are the keys to improving survival, and patients with necrotizing infections need an integrated multidisciplinary approach to management. It is adjusting with the infecting organism, the site of infection, and the effects from any toxins produced, and incorporating various clinical and laboratory parameters.

**MATERIALS AND METHODS**

**Source of Data**
This study was conducted comprising 50 patients of NF in Department of General Surgery and Microbiology at Katihar Medical College, Katihar (Bihar) for a period of 9 months between 2015 and 2016.

**Inclusion Criteria**
1. Patient has organisms cultured from tissue or discharge from affected site
2. Patient has purulent drainage at affected site
3. Patient has an abscess or other evidence of infection seen during surgical debridement
4. Patient has at least 2 of these signs or symptoms at the affected site with no other recognized cause: Localized pain or tenderness, redness, swelling, or heat.

**Collection and Processing**
Wound swab from all patients diagnosed to have NF was collected after surgical debridement. Blood culture (2 sets preferably) were done if there was any signs of bacteremia. The tissue was homogenized under sterile conditions and was cultured on blood and McConkey agar. The culture plates were incubated overnight at 37°C for aerobic growth. Bacterial growth was identified by the biochemical test and the resistance pattern by disc diffusion method according to Clinical and Laboratory Standards Institute guidelines. The tissue sample or the wound swab was inoculated immediately after collection in Robertson’s cooked meat media for further anaerobic culture and identification. Variables that were examined included age, sex, mode of presentation, site/location of infection, co-morbid illness, etiological factors, admitting diagnosis, investigations, microbiological characteristics, antibiotic sensitivity, and the treatment outcome.

**Methods of Collection of Data**
- Detailed history taking
- Clinical examination
- Investigations (routine laboratory investigation)
- Relevant special investigations
- Conservative management with meticulous dressing and if needed major surgical interventions with its outcome.

**RESULTS**

**Age**
Out of 50 cases studied, the youngest patient was 30 years of age and oldest was 79 years. The highest number of cases was found in the age group 51-60 years (36%), followed by 41-50 years (28%) (Table 1).

**Sex**
Out of the 50 cases studied under this series, the majority of the patients were male 46 (92%) and the contribution of female patients was 4 (8%) (Table 2).

**Sites of Involvement and Number of Patients Affected**
Lower limb was the most common site of involvement which was predominantly seen in calf region followed by involvement of both calf and foot (Table 3).

**Risk Factors**
Diabetes mellitus was the most common risk factor present in majority of the cases of NF (44%), followed by increasing age more than 60 years (24%). Hypertension was present in 10% of the cases. No identifiable risk factor was present in 12% of the cases (Table 4 and Figure 1).

**Clinical Features**
Tenderness was present in majority of the patients (94%) followed by edema (74%). Other features present were erythema of skin, woody hard texture of skin, skin vesicles and bullae, hypotension, fever, tachycardia, and altered mental status.

**Culture**
Culture in 38 patients (76%) showed positive growth, while no growth was present in 12 patients (24% of cases). Among culture positive patients, monomicrobial growth was present in 46% cases which were slightly more than patients with polymicrobial growth (30%) (Figure 2).
Microorganisms Isolated
Among the polymicrobial growth (30%), organisms isolated were a combination of Gram-positive organisms such as *S. aureus*, *Enterococcus faecalis*, and *Streptococcus pyogenes* and Gram-negative bacteria such as *E. coli*, *Pseudomonas aeruginosa*, *Klebsiella pneumonia*, and *Proteus vulgaris*. *P. aeruginosa* (46.67%) was the most common organism isolated among polymicrobial growth. While among the monomicrobial growth (46%), the most common organism isolated was *S. aureus* (43.48%), followed by *Klebsiella* (21.74%), while other organisms being *Pseudomonas*, *E. coli*, and *Streptococcus*. No growth was detected in 12 patients (24%).

Antimicrobial Sensitivity Testing
Among the antibiotic susceptibility pattern of isolates, maximum resistance pattern was found to cefixime and cotrimoxazole. Organisms were mostly sensitive to amikacin, gentamicin and ofloxacin. Also organisms were moderately sensitive to amoxicillin and clavulanic acid (Co-amoxycycl).

DISCUSSION
Being a surgical emergency with a high degree of morbidity and mortality, NF requires early recognition and aggressive debridement to avoid sepsis and subsequent death from it. Most of the studies have reported a mortality rate of 30-70%.\(^9\)\(^,\)\(^11\) NF has affected wide age group, but most commonly affected age of presentation was between age group 51 and 60 years (36%) and minimum in young age group of 21-30 years (2%) in our study. The incidence being more common male gender by far. The reason for male gender was most of them being agriculturist who used to work in field for long time and ignoring minor pricks and trauma leading to larger infected wound. Other associated
reason being lack of education, unhygienic environment, and lack of access to healthcare facilities in rural area. Among the sites involved, the most common site of involvement was the calf region (56%) followed by foot (14%). Diabetes mellitus was the most common risk factor present in majority of the cases of NF (44%), followed by increasing age more than 60 years (24%). These patients usually have a pre-existing disease which increases the susceptibility to infection. Most common ones are diabetes mellitus, age >60 years, hypertension, and chronic renal failure. Other factors being chronic liver disease and HIV infection. A number of co-morbidities are associated with NF. Clinicians should have a higher index of suspicion when patients with diabetes or liver cirrhosis present with cutaneous infection.

Diabetes mellitus was the most common risk factor present in majority of the cases in our study of NF (44%), followed by increasing age more than 60 years (24%). The presence of diabetes mellitus as the most common predisposing risk factor in our study is also consistent with other studies.

Culture in 38 patients (76%) showed positive growth, while no growth was present in 12 patients (24% of cases). Among culture positive patients, monomicrobial growth was present in 46% cases, which was slightly more than patients with polymicrobial growth (30%). In a study conducted by Goh et al., the overall positive wound culture rate was 76.5% which is very similar to our study.

In this study, among the polymicrobial growth (30%), organisms isolated were a combination of Gram-positive organisms such as S. aureus, E. faecalis, and S. pyogenes and Gram-negative bacteria such as E. coli, P. aeruginosa, K. pneumonia, and P. vulgaris. P. aeruginosa (46.67%), was the most common organism isolated among polymicrobial growth. While among the monomicrobial growth (46%), the most common organism isolated was E. coli and Streptococcus (43.48%), followed by S. aureus (34.78%) and Klebsiella (13.01%) while other organisms being Pseudomonas. No growth was detected in 24% of cases. Organisms common in polymicrobial infections in other studies were: Staphylococcus spp., Streptococcal spp., Bacteroides and E. coli. Among monomicrobial infections, S. pyogenes was found in the study by Nisbet et al., S. aureus was reported by Huang et al. In a study conducted by Mathew et al., 56.6% were monomicrobial and 44.4% were polymicrobial growth. Most common organism isolated was P. aeruginosa (23%) among polymicrobial growth followed by K. pneumonia (16%) and S. aureus (16%). E. coli and beta hemolytic Streptococcus is also reported to be an important cause of monomicrobial infection (45.6%) in NF in other studies.

Among the antibiotic susceptibility pattern of isolates, maximum resistance pattern was found to cefixime and co-trimoxazole. Organisms were mostly sensitive to amikacin, gentamicin and ofloxacin. Also organisms were moderately sensitive to amoxicillin and clavulanic acid (Co-amoxyclav). Control of diabetes with oral hypoglycemics and insulin, treatment of various co morbidities, use of appropriate antibiotics, and surgical debridement along with skin grafting and amputation wherever needed were the various modalities of treatment employed in these patients.

**CONCLUSION**

NF is a rapidly progressive disease with systemic toxicity and proves to be fatal if not treated. It is a surgical emergency, so requires aggressive approach. The presence of the infection should be determined by clinical findings and appropriate wound cultures and thus treatment should be based on culture reports. Sometimes culture reports are negative and in such cases molecular techniques may help in identifying microorganisms and thus helps in treatment. Patient education, proper care of feet, and a multidisciplinary approach is essential for patients with NF.

**REFERENCES**


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Analysis of Fine Needle Aspiration Cytology of Pediatric Thyroid Lesions: A Study from Western India

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Abstract

Background: Thyroid lesions are rare in childhood and youth and incidence of thyroid malignancy is higher in pediatric age group than in adults. As approach to thyroid lesions in general is multidisciplinary, fine needle aspiration cytology (FNAC) forms an important indispensable tool.

Objective: To analyze retrospective data of pediatric thyroid FNAC, identify spectrum of benign and malignant thyroid lesions and to evaluate its correlation with ancillary thyroid investigations.

Materials and Methods: Retrospective data of 37 pediatric thyroid FNAC in age group of 0-15 years was analyzed over a 4-year period from April 2012 to June 2016. Cytology findings from air dried and alcohol fixed smears stained with Giemsa and Papanicolaou stain respectively was correlated with ultrasonography (USG), thyroid function tests (TFTs), and anti-thyroid antibodies if present.

Results: Pediatric thyroid FNAC formed 2.43% of total thyroid FNAC done in the tertiary care center over 4 years period. Females formed the majority with female: male being 2.3:1. Benign thyroid lesions were seen in 33 (89.18%) cases comprising equal number of cases of nodular goiters and thyroiditis. Benign thyroid cyst including thyroglossal cysts formed 13.5% and well differentiated papillary thyroid carcinoma formed 5.4%. USG thyroid and TFTs correlated well with benign thyroid lesions.

Conclusion: FNAC forms an important diagnostic tool in analyzing pediatric thyroid lesions when used along with other multidisciplinary thyroid approaches. It forms a crucial tool in identifying malignancy and thereby any unnecessary surgery.

Key words: Paediatric, Thyroid, Cytology

INTRODUCTION

Pediatric fine needle aspiration cytology (FNAC) has always been a challenge technically as well as diagnostically due to wide variety of lesions at different age groups and at different sites.

Incidence of thyroid lesions in general population is 19-35%¹ and in pediatric age group as per the literature search has been 0.05-1.8%.² Although malignancy in thyroid lesions is <5% but can go up to 25% in childhood presentation of thyroid nodules. Thyroiditis presents as the most common childhood thyroid lesions or nodule (2-48%).³ Niedziela and Stevens et al. have reported 8-50% incidence of malignancy in childhood thyroid nodules in their comparative meta-analysis.³,⁴ Hence, we decided to evaluate pediatric thyroid lesions in a tertiary care center to identify the spectrum of thyroid lesions in childhood. Reporting criteria on FNAC of thyroid malignancy, thyroiditis, and nodular goiter remains the same as done in adult population.

Aims and Objectives

To analyze FNAC results of thyroid lesions in pediatric age group from 0 to 15 years over 4 years period from April 2012 to June 2016. To evaluate its association with thyroid...
function tests (TFTs), ultrasonography (USG) of thyroid, and anti-thyroid antibodies.

**MATERIALS AND METHODS**

The study was retrospective in nature. Data from cytology section of Department of Pathology in a tertiary care center were analyzed over a period of 4 years from April 2012 to June 2016. Study group comprised patients in 0-15 years who underwent a thyroid FNAC examination at our center. Prior consent was taken from parents or guardians for FNAC as patients were under 15 years of age. All thyroid FNAC beyond 15 years of age were excluded from the study. All FNAC were done under sonography guidance and using a 23 g needle. Ultrasound details, TFT were noted and analyzed. None of the cases had any post procedural complication. Air dried and alcohol fixed smears for Giemsa and Papanicolaou stains done respectively were evaluated. A detailed analysis of a total of 37 pediatric thyroid cases identified from a total of 1520 thyroid FNAC done over 4 years was carried out. Histopathology data was looked up for follow-up in all the surgical operated thyroid nodules.

**RESULTS**

Out of 1520 total thyroid FNAC performed over a period of 4 years, 37 were in pediatric age ranging from 6 to 15 years of age. Females outnumbered over males with 70.3% (26) females as compared to 29.7% (11) males. The female to male ratio was 2.3:1 (Figure 1). The FNAC results showed majority of cases, i.e. 33 (89.18%) having benign cytological features of which maximum were formed by nodular goiters 14 (37.8%) cases and 14 (37.8%) cases of thyroiditis including a single case of Hashimoto’s thyroiditis. All cases of thyroiditis showed cellular smears with clusters of benign thyroid follicular cells being destroyed by lymphocytes (Figure 2). The benign thyroid lesions also included 5 (13.5%) cases of colloid cysts including three cases of thyroglossal cysts. One case showed features of grave’s disease. Papillary carcinoma was identified in two (5.40%) cases. Smears from papillary carcinoma showed cellular smears with scant colloid, clusters of thyroid follicular cells with clear nuclei, powdery chromatin, intranuclear inclusions, and nuclear grooves (Figure 3). Both the cases underwent total thyroidectomy and showed papillary carcinoma on histopathology examination. No opinion was given in 2 cases. Goiter was seen in 14/37 (37.8%) cases with 11 cases seen in age group of 10-15 years (Table 1).

Applying Bethesda categories on reporting of thyroid FNAC, 33 (91.6%) cases had Bethesda category 2, Bethesda category 5 for the two cases of neoplastic lesions, and one benign thyroid cytology showed Bethesda category 1. No opinion possible in two cases.

**USG Results**

Thyroid sonography details were available in 33/37 cases. Majority showed bulky thyroid in 10/37 (27.02%) cases, all of which showed thyroiditis on FNAC. Single thyroid nodule was noticed in 5 cases which composed of two cases of neoplasm and rest nodular goiter. Cystic lesions were identified in 5 cases which includes...
three cases of thyroglossal cyst where thyroid gland was normal.

**Laboratory Results**

TFTs were available in 31/37 patients, they were correlated with thyroid lesions. Majority of the lesions were euthyroid 22 (70.9%) cases followed by hypothyroid 7 (22.5%) cases and hyperthyroid 2 (6.4%) cases. The euthyroid included 12 cases of nodular goiter, 6 cases of lymphocytic thyroiditis, 2 cases of cysts, and 2 cases of neoplasms. All 7 cases that were hypothyroid on TFT were diagnosed as lymphocytic thyroiditis on FNAC. Two cases of hyperthyroid results on TFT included 1 case each of lymphocytic thyroiditis and Grave’s disease (Table 2).

**DISCUSSION**

Thyroid lesions vary widely in various age groups with a majority being a wide spectrum of benign lesions over malignancies comprising of nodular goiters with or without cystic change, thyroiditis, solitary colloid cysts, and developmental anomaly such as thyroglossal cyst. Advent and usage of FNAC in evaluation of thyroid lesions has found to be superior when used along with well-established battery of non-invasive diagnostic methods such as USG thyroid, TFTs, and anti-thyroid antibodies especially in cases of malignancies.

FNAC of thyroid in adult population has been a well-established tool in evaluation of thyroid nodules which has drastically brought down the necessary surgical resections. The need for using the same in pediatric population brings down its prevalence to 0.05-1.8%,

This retrospective study was undertaken to identify spectrum of thyroid lesions in pediatric age group as they are challenging with respect to clinical presentation, common age related thyroid disorders, high incidence of thyroid malignancies, and challenges during surgery too. Literature search on pediatric thyroid FNAC series studied showed that these lesions are more common in females. In our study, majority of pediatric thyroid lesions evaluated were found be more common in females (70.3%) with female: male being 2.3:1. Similar results were found in thyroid series analyzed by Kacar et al. who had 66.6% females in his study. Siddigowda et al. found higher incidence in females with higher female: male in various age groups more towards youth. Distribution of lesions in both childhood and youth is found to behave like a preponderance of benign thyroid lesions with thyroiditis being more common in childhood compared to adults.

In the present study, 89.1% cases were benign thyroid lesions of which 37.8% were of thyroiditis. Majority of cases of thyroiditis were in the age group of 10-15 years. Vasudev et al. had 36% cases of thyroiditis in age group of 7-12 years and 75% in age group between 12 and 15 years. Thereby suggesting a higher incidence in adolescent age group. A single case each of Hashimoto’s thyroiditis and grave’s disease were seen in 15 years and 13-year-old females respectively.

We had 3 (8.1%) cases of thyroglossal cyst, youngest was in a 7-year-old female. Pindicura et al. had 12% thyroglossal cyst in his study of 389 pediatric thyroid cases in age group of 0-14 years. It is essential to identify these lesions on FNAC and radiology for the rare papillary carcinomas arising from thyroglossal cyst. There is 1% incidence of papillary carcinoma arising in thyroglossal cyst.

Although the prevalence of pediatric thyroid lesions is 10-fold less, the incidence of well differentiated thyroid neoplasms is much more than in adults. Our study had 2 (5.4%) cases of papillary carcinoma seen in a 6-year-old female and in a 15-year-old male. Pindicura et al. reports an incidence of 2-50% thyroid neoplasms in pediatric age group.

**CONCLUSION**

FNAC being the most cost effective and outpatient department procedure serves as a useful diagnostic tool in evaluation of differential diagnosis of pediatric thyroid lesions used along with other non-invasive diagnostic methods of thyroid studies such as TFTs, radiology, and anti-thyroid antibodies. Benign thyroid lesions form the majority with a steady rise in thyroiditis as age advances. Awareness and identification of thyroid malignancies in solitary thyroid nodules or in thyroglossal cysts is essential due to higher incidence of malignancy in childhood thyroid
lesions and better prognosis. We highlight and suggest pediatric thyroid lesions form an important part in thyroid FNAC and encourage more ancillary techniques to be used to cytology specimens.

REFERENCES

Bacteriological Profile of Burn Wounds and Their Antibiotic Susceptibility Pattern in a Tertiary Care Hospital

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Abstract

Introduction: Burn wound provides an ideal site to bacterial colonization or infection, leading to morbidity and mortality. Early identification of infection provides improved management and leads to better prognosis.

Purpose: The aim of this study was to identify the bacteriological profile of burn wounds and their antibiotic susceptibility pattern in patients admitted in the burn unit of Bankura Sammilani Medical College. A prospective study was done in the burn unit and bacteriology laboratory of the department of microbiology for 6 months.

Methods: Swabs were collected from the wounds of a total of 72 patients admitted in burn unit, after taking a thorough history and demographic data. The swabs were inoculated in appropriate culture media, and identification was done following the standard procedure.

Results: Pseudomonas aeruginosa (30%) and Staphylococcus aureus (30%) were the most common isolate from burn wounds followed by Klebsiella spp. (20%).

Conclusion: The finding of the study will be helpful for identifying the common bacteria causing burn wound infection and also to take proper precautions to prevent the emergence of antibiotic-resistant bacteria.

Key words: Antibiotic susceptibility, Bacteriological profile, Burn wounds, Methicillin-resistant Staphylococcus aureus

INTRODUCTION

Injuries and deaths due to burn are a global concern with regards to public health, accounting for an estimated 265,000 deaths annually. The majority of these occur in low- and middle-income countries and almost half occur in the WHO South-East Asia Region.¹ Approximately, 75% of deaths occur primarily because of inhalation of soot or absorption of carboxyhemoglobin in the blood, but burn wound sepsis remains an important infectious complication of burn.²³ In India, in the year 2013, a total of 22,177 (5.9%) deaths and 2391 injuries occurred as a result of some form of accidents due to fire. Fire accidents constituted 5.5% of the un-natural causes of accidental deaths, of which 65.7% of those killed were females who out-numbered males (34.3%).⁴ The most common causes of work-related burns are contacted with chemicals or hot liquids, followed by electricity and then molten or hot metals.⁵

The primary insult from a burn is the wound itself, which has three characteristic areas of involvement.⁶ The first associated area of the wound is the zone of coagulation nearest the heat source and includes dead tissue forming the burn eschar. Adjacent to this zone is the second area, known as the zone of stasis, which is viable but at risk
of ischemia because of perfusion defects. The zone of hyperemia is the third area, which consists of relatively normal skin with increased blood flow and vasodilatation and minimal cellular injury. Overall, the primary concern of burn wound injuries is the moist, protein rich eschar, which is an ideal environment for microorganisms, and its avascular nature prevents immune cells and systemically administered antibiotics from being delivered. Typically, the burn surface is sterile immediately following thermal injury, but after 48 h the wound is colonized with skin pathogens that typically reside in sweat glands and hair follicles before the burn.

Risk factors for burn wound colonization or infection are the size of the burn wound, i.e., the percentage of total body surface area (TBSA) burnt and the duration of hospitalization.

Severe burn causes a mechanical disruption of the skin allowing microbes to penetrate to the deeper tissues that act as a favorable factor for bacterial multiplication leading to infection. The organisms responsible for infections in patients with severe burns may be endogenous or exogenous and include bacteria, fungus, and viruses which can change over time in the individual patient.

Microorganisms are probably transmitted to the burn wound surfaces of recently admitted patients by the hands of healthcare personnel and by fomites. The gastrointestinal tract continues to be a potential reservoir for microorganisms that colonize the burn wound surface. It is likely that endogenous microorganisms continue to be transmitted to burn wound surfaces by feces. Nosocomial infection rates in burn wounds have been reported from 77 to 90 infections/100 patients or an incident density of 32-48 infections/1000 patient-days. Improvements in the care of patients who suffer burns, especially initial burn shock resuscitation, airway management, burn wound care, and infection control practices has resulted in remarkably improved survival rates.

Outcomes appear worse with polymicrobial infections.

Various bacteria can cause infection of burn wound. Historically, Streptococcus pyogenes was the most frequently recovered pathogen, but this has been replaced with Staphylococcus aureus and Gram-negative pathogens, such as Pseudomonas aeruginosa, Klebsiella pneumoniae, and Acinetobacter baumannii, with higher resistance profiles as patients stay in the hospital longer.

There is no data regarding the bacteriological profile of burn wounds and their antibiotic susceptibility pattern in Bankura district and surrounding areas of West Bengal. The present study is undertaken to identify the bacteriological profile of burn wounds and their antimicrobial susceptibility pattern in patients admitted in Bankura Sammilani Medical College. This study will be helpful to determine the predominant microorganisms causing infection in the burn care units, and the study of their antimicrobial susceptibility pattern will help to formulate the antibiotic policy to provide relief, quick wound healing, and better management of the patients.

### MATERIALS AND METHODS

This prospective study was done in the burn unit and bacteriology laboratory of the Department of Microbiology for a period of 6-months starting from 1st November 2015 to 30th April 2016. After ethical clearance, swabs were collected from a total of 72 patients admitted to burn unit. A written informed consent was taken from each patient before collecting the swab. The patients with pre-existing chronic diseases such as diabetes mellitus and tuberculosis were excluded from the study. A thorough history was taken regarding the demographic data such as age, sex, occupation, address of the patient, and mode of burn. For each patient, swabs were collected on the date of admission, and after that at 48 h interval for the duration of stay of the patient, till discharge or death of the patient. The patients, who were dead or discharged before 48 h of admission, were excluded from our study.

After removal of the bandage, the site of burn was thoroughly washed with normal saline. Remains of topical antibacterial agents used on the wound were washed. Sterile cotton swabs were smoothly rolled over the wound area aseptically, and the discharge was collected. The swabs were immediately transported to the bacteriology laboratory in sterile test tubes and inoculated without delay on MacConkey agar (HiMedia Laboratories Pvt. Ltd., Mumbai) and blood agar, using a sterile loop. After aerobic incubation at 37°C for 24 h, the Petri plates were inspected for growth of bacteria in the form of colonies. Those, which showed no colony, were noted down as no growth. The media, which showed the appearance of colonies, were processed following the standard bacteriological procedures. Colony characteristics of each type were recorded. Gram-staining was done from the colonies, and based on the findings of that, identification of bacterial isolates was done by conventional biochemical tests for identification.

Antimicrobial susceptibility testing of the bacterial isolates was done by disk diffusion technique (using Kirby Bauer's method) on Mueller-Hinton agar (MHA) (HiMedia Laboratories Pvt. Ltd., Mumbai) as per Clinical and Laboratory Standards Institute (CLSI) guidelines.
Inoculum for each isolate was prepared by direct colony suspension in nutrient broth, the turbidity of the broth was adjusted to a 0.5 McFarland standard suspension, which contains approximately $1.4 \times 10^8$ colony-forming units/ml. The MHA plates were inoculated and then incubated at 37°C for overnight. On the next day, MHA plates were examined, the zone of inhibition was noted by measuring with a ruler held against the back of Petri plate and the sensitivity pattern of the bacterial isolates to various antibiotics were noted. Methicillin-resistant *S. aureus* (MRSA) strains were detected by following the CLSI guideline.

The data were tabulated and statistical analyses of the data were done using SPSS Statistics 19.0 (IBM Corp. Released 2010. IBM SPSS Statistics for Windows, Version 19.0. Armonk, NY: IBM Corp.). Qualitative and quantitative data were expressed as frequency and percentage. Association between two or more qualitative variables was analyzed using Chi-square test. A two-sided $P < 0.05$ was considered to be statistically significant.

**RESULTS**

A total of 136 samples were collected from burn wounds of 72 patients. 120 swabs showed growth and 16 swabs showed no growth after 24 h of incubation. Samples were collected from 55 females (76.4%) who were more affected due to burn than that of males (23.6%), who were 17 in number.

Among the patients from whom samples were collected, 33.3% (24/72) were of 21-30 years age group, 25% (18/72) were of 31-40 years age group, and 19.4% (14/72) were of 11-20 and 16.7% (12/72) were of 41-50 years age group. Patients of 10 years or less and more than 50 years were few in number which was 2.8% (2/72) each. Table 1 shows the distribution of patients according to age.

Regarding the TBSA of burn, 25% (18/72) had TBSA of burn in the range of 61-80%, 22.2% (16/72) had TBSA in between 1-20% and 21-40% each; 16.7% (12/72) and 13.9% (10/72) had TBSA of 41-60% and 81-100%, respectively.

Among the bacteria isolated from burn wounds, 56.67% (68/120) was Gram-negative bacilli and 43.33% (52/120) was Gram-positive cocci. Graph 1 shows the distribution of bacteria isolated from burn wound. In the present study, *P. aeruginosa* (30%) and *S. aureus* (30%) were the most common isolates from burn wounds followed by *Klebsiella* spp. (20%). Of the 36 isolates of *S. aureus*, 20 were tested to be MRSA, and 16 were Methicillin-susceptible *S. aureus* (MSSA).

The antimicrobial susceptibility pattern of the Gram-negative and Gram-positive isolates is shown in Table 2 and Graph 2, respectively.

**DISCUSSION**

A total of 136 samples were collected for the study, of which, 120 samples showed growth. So, in this study, the overall isolation rate was 88.23% (120/136), which was near to the isolation rate of a study on burn wound infection done in Mumbai (86.28).

Regarding the sex distribution of the samples collected, females (76.4%) were more in number than males (23.6%),

![Graph 1: Distribution of bacterial isolates from burn wounds](image1)

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Number of patients</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-10</td>
<td>2</td>
<td>2.8</td>
</tr>
<tr>
<td>11-20</td>
<td>14</td>
<td>19.4</td>
</tr>
<tr>
<td>21-30</td>
<td>24</td>
<td>33.3</td>
</tr>
<tr>
<td>31-40</td>
<td>18</td>
<td>25.0</td>
</tr>
<tr>
<td>41-50</td>
<td>12</td>
<td>16.7</td>
</tr>
<tr>
<td>&gt;50</td>
<td>2</td>
<td>2.8</td>
</tr>
<tr>
<td>Total</td>
<td>72</td>
<td>100</td>
</tr>
</tbody>
</table>

![Graph 2: Antimicrobial susceptibility pattern of Gram-positive bacteria isolated from burn wound of patients](image2)

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Number of isolates</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colistin</td>
<td>20</td>
<td>30%</td>
</tr>
<tr>
<td>Vancomycin</td>
<td>30</td>
<td>30%</td>
</tr>
<tr>
<td>Gentamicin</td>
<td>18</td>
<td>16.7%</td>
</tr>
<tr>
<td>Clindamycin</td>
<td>22</td>
<td>18.3%</td>
</tr>
<tr>
<td>Linezolid</td>
<td>26</td>
<td>21.7%</td>
</tr>
<tr>
<td>Erythromycin</td>
<td>14</td>
<td>11.1%</td>
</tr>
</tbody>
</table>
Table 2: Antimicrobial susceptibility pattern of Gram-negative bacteria isolated from burn wound of patients

<table>
<thead>
<tr>
<th>Name of the antibiotics used</th>
<th>Pseudomonas aeruginosa (36)</th>
<th>Klebsiella spp. (24)</th>
<th>Proteus mirabilis (4)</th>
<th>Citrobacter freundii (2)</th>
<th>Enterobacter cloacae (2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gentamicin</td>
<td>16 (44.4)</td>
<td>10 (41.7)</td>
<td>4 (100)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Polymyxin B</td>
<td>20 (55.6)</td>
<td>20 (83.3)</td>
<td>4 (100)</td>
<td>2 (100)</td>
<td>2 (100)</td>
</tr>
<tr>
<td>Piperacillin-tazobactam</td>
<td>4 (11.1)</td>
<td>4 (16.7)</td>
<td>4 (100)</td>
<td>2 (100)</td>
<td>2 (100)</td>
</tr>
<tr>
<td>Levofloxacin</td>
<td>20 (55.6)</td>
<td>20 (83.3)</td>
<td>2 (50.0)</td>
<td>0</td>
<td>2 (100)</td>
</tr>
<tr>
<td>Meropenem</td>
<td>20 (55.6)</td>
<td>12 (50.0)</td>
<td>4 (100)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Netilmicin</td>
<td>28 (77.8)</td>
<td>18 (75.0)</td>
<td>4 (100)</td>
<td>0</td>
<td>2 (100)</td>
</tr>
<tr>
<td>Cefazidime</td>
<td>20 (55.6)</td>
<td>20 (83.3)</td>
<td>4 (100)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Cefpodoxime</td>
<td>16 (44.4)</td>
<td>20 (83.3)</td>
<td>4 (100)</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

with a female to male ratio of 3.23:1. This can be attributed to females being more exposed to household fire while cooking and also suicidal and dowry deaths. This finding of female predominance in burn patients correlated with other studies done in different hospitals in India.25,26

The patients belonging to 21-30 years age group (33.33%) were most affected followed by age group of 31-40 years (25%). This finding may be due to the reason that most of the patients admitted to the burn unit were in this age group and also because these are the years of life more exposed to working with fire, both household and occupational.

The most of the patients who developed infection had burn of 81-100% of TBSA. Therefore, the more was the TBSA, the more was the risk of colonization and proliferation of various bacteria in burn wound.

Gram-negative bacilli (56.67%) were isolated more frequently than Gram-positive cocci (43.33%). According to the report published in various studies around the world, *P. aeruginosa* was the most common pathogen.27-30 On the other hand, according to some other studies, *S. aureus* was the predominant organism isolated from burn wounds.31,32 In this study, *P. aeruginosa* (30%) and *S. aureus* (30%) were equally isolated from culture of the wound swabs.

Among the isolated *S. aureus*, 55.56% (20/36) were MRSA and 44.44% (16/36) were MSSA. So, the most of the Gram-positive bacterial infections in burn wound were caused due to MRSA. This percentage of MRSA in this study was more than another study on burn wound infection, where it was shown that 39.8% isolates were MRSA.33

The strength of this study was that it would be helpful for better patient care in burn units, and precautionary actions to prevent the emergence and spread of resistant microorganisms can be undertaken.

The limitation of the study was that it was conducted for a short span of time; it would have been better if the study could be performed for a longer duration with a larger sample size. Furthermore, because some of the patients were dead or discharged before 7 days, we could not take another sample from them after 7 days of admission to know the bacteriological profile.

**CONCLUSION**

The result of the study is helpful for identifying the common causes of burn wound infections in this region. Moreover, it will be helpful to select the appropriate antibiotics in appropriate dosage to control the infection and also to prevent the emergence of antibiotic-resistant bacteria. *P. aeruginosa* and *S. aureus* were the predominant organisms in burn wound infections. According to the Centers for Disease Control and Prevention, some factors are responsible for transmission of MRSA. These factors, referred to as the 5 C’s, are as follows: Crowding, frequent skin-to-skin contact, compromised skin (i.e., cuts or abrasions), contaminated items and surfaces, and lack of cleanliness.34 High degree of occurrence of MRSA observed in this study necessitates some essential measures such as proper care of the wound, contact isolation (patients infected with MRSA), implementation of strict hospital infection control measures such as meticulous hand washing and prevention of sharing of personal items by patients, to minimize the transmission and infection of the patients in the burn unit, so as to reduce the morbidity and mortality of the patients.

**REFERENCES**


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Prevention of Post-operative Wound Infection and Sepsis in Abdominal Surgery

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Abstract

Background and Objectives: Wound infection in abdominal surgery is a common surgical complication that an abdominal surgeon comes across in his day to day career. Even today in the modern antibiotic era, the incidence of wound infection has not significantly come down. Here is an attempt to made to enlighten the various causes of wound infection in each abdominal procedures, the skill full ways of preventive measures to eradicate them, the bacteriology, pathophysiology, and epidemiology are reviewed and preventive aspects discussed in detail.

Materials and Methods: Out of 2000 cases operated for abdominal problems, we have taken 350 patients in a randomized fashion for study. Factors were tabulated and statistically analyzed to study their contribution.

Results: In our study, the overall wound infection rate was 12.5%. Emergency cases had more infection than elective. Infection rate was higher if the age is >60 years. The wound infection rate is high up to 30% with the patient who stayed more than 1 month. Increased infection rate seen in skin preparation done more than 6 h before surgery.

Conclusion: Prevention of wound infection and sepsis in abdominal surgery shortens the hospital stay, minimize the expenditure, and avoids the morbidity and mortality. It is a joint responsibility of the surgical team paramedical staff, patient, and also the bacteriologists.

Key words: Antibiotic prophylaxis and skin preparation, Emergency and elective surgeries, Sepsis

INTRODUCTION

The biological state of human being is not a germ-free environment.¹ It is a symbiotic relationship between the host defense mechanism and its microbial flora. If any alteration occurs, infection will be the end result. Even today in the modern antibiotic era, the incidence of wound infection has not significantly come down.² Tracing the history of wound infection in abdominal procedures, we can see retrospectively that certain fundamental requirement to be fulfilled first for better understanding and prevention. First, all the normal biological flora of the abdomen is to be understood. Second, the source of sepsis is to be identified, and third, the preventive measures at every step - Pre-, intra-, and post-operative periods have to be carried out strictly.

After world war, it has been understood that despite antiseptic techniques, wound become infected either by initial contamination or cross infection.¹² Then, came the beginning of antibiotic era. The greatest advance in abdominal bacteriology in the last decade has been the realization of anaerobic organisms as a cause of sepsis.

MATERIALS AND METHODS

Out of 2000 cases operated for abdominal problems, we have taken 350 patients in a randomized fashion for study. Factors were tabulated and statistically analyzed to study their contribution. The following data were included in the study:

1. **Age/sex**
   - Date of admission
   - Date of surgery.
2. Diagnosis - Procedure done  
• Duration of procedure  
• Post-operative study  
• Suture removal/presence of post-operative infection  
• Wound culture sensitivity.

RESULTS AND OBSERVATIONS

In spite of the strict aseptic precautions, antibiotic prophylaxis, and meticulous surgical techniques, prevention of wound infection is still a problem to the surgeon. In our study of 350 patients including 200 elective and 150 emergency cases, we met with an overall infection rate of 12.5%.

Referring to Table 1, we had more number of infected patients in an emergency (25) rather than elective (18). This may be attributed to inadequate preparation of the patient, inadequate antibiotics, failure in aseptic precautions, and more complications in emergency cases.

Referring to Table 2, even though the number of wound infection were relatively more among the male sex compared to female, there is no significant influence of sex among the incidence of wound infection rate.

Table 1: Comparison for elective and emergency

<table>
<thead>
<tr>
<th>Abdominal surgical procedure</th>
<th>Total cases</th>
<th>Number of cases infected</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall procedures</td>
<td>350</td>
<td>43</td>
<td>12.29</td>
</tr>
<tr>
<td>Elective</td>
<td>200</td>
<td>18</td>
<td>9</td>
</tr>
<tr>
<td>Emergency</td>
<td>150</td>
<td>25</td>
<td>16.67</td>
</tr>
</tbody>
</table>

Table 2: Number of infected cases in female and male

<table>
<thead>
<tr>
<th>Sex</th>
<th>Total cases</th>
<th>Number of cases infected</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>Total</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Elective</td>
<td>150</td>
<td>11</td>
<td>7.33</td>
</tr>
<tr>
<td>Emergency</td>
<td>110</td>
<td>22</td>
<td>20</td>
</tr>
<tr>
<td>Female</td>
<td>Total</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Elective</td>
<td>50</td>
<td>7</td>
<td>14</td>
</tr>
<tr>
<td>Emergency</td>
<td>40</td>
<td>3</td>
<td>7.5</td>
</tr>
</tbody>
</table>

One of the most common sources of wound infection is acquired through a hospital stay from multiple antibiotic resistant strains such as *Staphylococcus aureus* and *Pseudomonas* in patients own site (Table 4).

Regarding the influence of age on wound infection, higher infection seen after the 6th decade, which may be due to low immunological and nutritional status of the patient. Intact those infected cases were from the emergency group because of the associated medical illness and lack of pre-operative workup. However, no infected cases in elective group due to adequate pre-operative workup, antibiotic prophylaxis (Table 3).

Regarding the influence of pre-operative stay in hospital, the wound infection rate is high up to 30% with the stay more than 1-month duration. This proves that reducing the number of days of stay will definitely reduce the infection rate.

Prolonged surgical time increases the incidence of wound infection rate, especially wound dehiscence or burst abdomen. In our study, we met with an infection rate of 27% in 15 surgeries lasting for more than 2 h when compared with the group of <2 h. We also found that there is little increase in the infection rate in <1 h group also about 21%. This can be attributed to the inadequate skin preparation, improper hemostasis, peritoneal lavage, proper drainage, and rough surgical techniques. So, these results tell us that the surgeon should take adequate time for preparation, perfect hemostasis, debridement, drainage, gentle handling of tissues, strict aseptic precautions, and laparoscopic procedures will minimize the operation time (Table 5).

In abdominal surgeries, the main source of infection is from endogenous contamination both aerobic and anaerobic organisms in one study; the sensitivity of pus showed mainly *Klebsiella*, *Escherichia coli*, and *S. aureus* is the most common multiple organisms seen in 5 cases. We have done cultures of peritoneal fluid in 12 cases. *E. coli* growth seen in two cases no growth in 5 cases. Multiple organisms seen in 5 cases (Table 6).

Table 7 depicts the influence of the type of surgical procedures on infection rates. Our study proved that...
infection rate is more in bowel perforation, appendicectomy, and colorectal surgeries. More infection rate is seen in infected and contaminated dirty wounds. Wound infection rate in relation to the surgical team shows a relatively low incidence (7%) among the group operated by the senior personnel. Because of his/her vast experience, skilled techniques, and strict aseptic precautions were achieved during surgery.

Regarding hair removal on skin preparation of the patient, we had less infection rate when shaving was done within ½ h before surgery (emergency - 10%, elective - 5%). We had no infection rate when there was sparse hair. Increased incidence of infection in shaving patients more than 6 h before surgery (Table 8).

Antibiotic prophylaxis is one of the mainstays in the prevention of wound infection. In one study of short-term pre-operative preparation using ampicillin or cefotaxime + metronidazole showed an infection rate of 12%, but the infection rate is comparatively high about 22% seen in antibiotics used postoperatively. This indicates that perioperative parenteral antibiotics maintain a better therapeutic levels during surgery (Table 9).

The wound infection in contaminated cases is mainly a subcutaneous problem. Various techniques have been employed to minimize the severity of contamination to minimize the infection rate. We have employed primary

**Table 4: Number of days in preoperative stay in the hospital**

<table>
<thead>
<tr>
<th>Pre-operative stay in hospital (days)</th>
<th>Total cases</th>
<th>Number of cases infected</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>0*</td>
<td>110</td>
<td>20</td>
<td>18.18</td>
</tr>
<tr>
<td>0-7</td>
<td>120</td>
<td>8</td>
<td>6.67</td>
</tr>
<tr>
<td>8-14</td>
<td>54</td>
<td>6</td>
<td>11.11</td>
</tr>
<tr>
<td>15-21</td>
<td>22</td>
<td>2</td>
<td>9.09</td>
</tr>
<tr>
<td>22-30</td>
<td>13</td>
<td>4</td>
<td>30.77</td>
</tr>
</tbody>
</table>

*All acute emergencies

**Table 5: Infection rate in relation to time of surgery**

<table>
<thead>
<tr>
<th>Duration of surgery</th>
<th>Total cases</th>
<th>Number of cases infected</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Up to 30 min</td>
<td>44</td>
<td>6</td>
<td>13.64</td>
</tr>
<tr>
<td>30 min-1 h</td>
<td>116</td>
<td>24</td>
<td>20.69</td>
</tr>
<tr>
<td>1-2 h</td>
<td>98</td>
<td>16</td>
<td>16.33</td>
</tr>
<tr>
<td>&gt;2 h</td>
<td>15</td>
<td>4</td>
<td>26.67</td>
</tr>
</tbody>
</table>

**Table 6: Types of infection and antibiotic sensitivity**

<table>
<thead>
<tr>
<th>Organisms</th>
<th>Number of cases (%)</th>
<th>Antibiotics–highly sensitive</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Amoxicillin</td>
</tr>
<tr>
<td>S. aureus</td>
<td>5 (10.4)</td>
<td>+</td>
</tr>
<tr>
<td>E. coli</td>
<td>14 (29.2)</td>
<td>+</td>
</tr>
<tr>
<td>Proteus</td>
<td>5 (10.4)</td>
<td>+</td>
</tr>
<tr>
<td>Klebsiella</td>
<td>15 (31.3)</td>
<td>+</td>
</tr>
<tr>
<td>Pseudomonas</td>
<td>8 (16.7)</td>
<td>+</td>
</tr>
<tr>
<td>Peptococci</td>
<td>1 (2.1)</td>
<td>+</td>
</tr>
<tr>
<td>Multiple organism</td>
<td>5 (10.4)</td>
<td>+</td>
</tr>
<tr>
<td>No growth</td>
<td>3 (6.3)</td>
<td>+</td>
</tr>
</tbody>
</table>

GM: Gentamicin, S. aureus: Staphylococcus aureus, E. coli: Escherichia coli

**Table 7: Infected case versus different surgical procedure**

<table>
<thead>
<tr>
<th>Surgical procedure done</th>
<th>Total cases</th>
<th>Number of cases infected (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elective</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gastric</td>
<td>15</td>
<td>2 (13.33)</td>
</tr>
<tr>
<td>Small bowel</td>
<td>3</td>
<td>1 (33.33)</td>
</tr>
<tr>
<td>Colorectal</td>
<td>5</td>
<td>2 (40.00)</td>
</tr>
<tr>
<td>Appendicectomy</td>
<td>40</td>
<td>6 (15.00)</td>
</tr>
<tr>
<td>Biliary</td>
<td>5</td>
<td>2 (40.00)</td>
</tr>
<tr>
<td>Inguinal hernia repair</td>
<td>110</td>
<td>6 (5.45)</td>
</tr>
<tr>
<td>Incisional hernia repair</td>
<td>17</td>
<td>3 (17.65)</td>
</tr>
<tr>
<td>Lumbar sympathectomy</td>
<td>5</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Emergency</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Appendicectomy</td>
<td>64</td>
<td>10 (15.63)</td>
</tr>
<tr>
<td>DU perforation</td>
<td>40</td>
<td>12 (30.00)</td>
</tr>
<tr>
<td>Ileal perforation</td>
<td>5</td>
<td>3 (60.00)</td>
</tr>
<tr>
<td>Strangulated hernia</td>
<td>20</td>
<td>2 (10.00)</td>
</tr>
<tr>
<td>Acute int. obstruction</td>
<td>9</td>
<td>4 (44.44)</td>
</tr>
<tr>
<td>Abdominal trauma</td>
<td>10</td>
<td>2 (20.00)</td>
</tr>
</tbody>
</table>

DU: Duodenal
closure with closed suction drain and outcome of results were encouraging when compared to primary closure without drain where the infection rate is high. The drains were brought out through the separate stab wound away from the main site. Drains were removed 2-5 days later depending on the nature of surgery (Table 10).

In our study, we have seen two cases of laparotomies done for severe peritonitis (septic abortion and gangrenous bowel). Wound is not sutured in layers. Skin closed with few loose stitches. After 2 days, the wound opened and thorough was given. This procedure was repeated at least 3 times. After sepsis was controlled, the wound was closed in layers. Skin approximated (Table 11).

A note on complication Table 13 depicts that one case of burst abdomen in the emergency cases. Out of 43 infected cases, only 20 patients turned up or regular follow-up. There was one case of an incisional hernia following laparotomy for a strangulated hernia.

**CONCLUSION**

Prevention of wound infection and sepsis in abdominal surgery shortens the hospital stay, minimize the expenditure of the patient, and avoids the morbidity and mortality. It is a joint responsibility of the surgical team paramedical staff, patient, and also the bacteriologists.

From our study, we are able to draw the following conclusions into focus:

1. A thorough pre-operative preparation of the patient, especially
   - Obese patients to be persuaded to reduce their weight before surgery
   - Associated skin problems and systemic illness to be taken care of
   - Antitetanus prophylaxis is a must
   - Adequate bowel preparation.

2. Perioperative short-term antimicrobial prophylaxis to be practiced in all elective and emergency cases

3. Pre-operative hospital stay in elective cases and duration of surgery in emergency cases to be cut short

4. Surgical techniques and principles may be improved by;

---

**Table 8: Infection rate versus surgical skill**

<table>
<thead>
<tr>
<th>Surgeon</th>
<th>Total cases</th>
<th>Number of cases infected (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unit chief</td>
<td>52</td>
<td>4 (7.69)</td>
</tr>
<tr>
<td>Assistants</td>
<td>220</td>
<td>37 (16.82)</td>
</tr>
<tr>
<td>PG</td>
<td>78</td>
<td>15 (19.23)</td>
</tr>
</tbody>
</table>

**Table 9: Pre-operative hair removal**

<table>
<thead>
<tr>
<th>Hair removal</th>
<th>Total cases</th>
<th>Number of cases infected (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No hair removal</td>
<td>4</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Shaving</td>
<td></td>
<td></td>
</tr>
<tr>
<td>½ h before surgery</td>
<td>100</td>
<td>10 (10)</td>
</tr>
<tr>
<td>2 h before surgery</td>
<td>50</td>
<td>7 (14)</td>
</tr>
</tbody>
</table>

**Table 10: Comparative study of DT and without DT**

<table>
<thead>
<tr>
<th>Method of closure</th>
<th>Total cases</th>
<th>Number of cases infected (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary closure with DT</td>
<td>84</td>
<td>10 (11.90)</td>
</tr>
<tr>
<td>Primary closure without DT</td>
<td>76</td>
<td>15 (19.74)</td>
</tr>
<tr>
<td>Laparotomy</td>
<td>2</td>
<td>-</td>
</tr>
</tbody>
</table>

**Table 11: Study of organisms in peritoneal fluid**

<table>
<thead>
<tr>
<th>Peritoneal aspirate</th>
<th>Number of cases sent for c/s</th>
<th>Organisms grown</th>
</tr>
</thead>
<tbody>
<tr>
<td>Perforated peptic ulcers</td>
<td>6</td>
<td>Multiple organisms in 5 cases</td>
</tr>
<tr>
<td>Perforated appendix</td>
<td>2</td>
<td>E. coli present in 2 cases</td>
</tr>
<tr>
<td>Gangrenous small bowel</td>
<td>4</td>
<td>No growth in 5 cases</td>
</tr>
</tbody>
</table>

**Table 12: Comparative study of open and close dressings**

<table>
<thead>
<tr>
<th>Dressings</th>
<th>Total cases</th>
<th>Number of cases infected (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Occlusive dressings</td>
<td>20</td>
<td>4 (20)</td>
</tr>
<tr>
<td>Exposure technique</td>
<td>100</td>
<td>11 (11)</td>
</tr>
</tbody>
</table>

**Table 13: Various complications following surgery**

<table>
<thead>
<tr>
<th>Complications</th>
<th>Number of cases followed</th>
<th>Incidence</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Burst abdomen</td>
<td>43</td>
<td>1</td>
<td>2.1</td>
</tr>
<tr>
<td>Bowel fistula</td>
<td>43</td>
<td>4</td>
<td>8.33</td>
</tr>
<tr>
<td>Post-operative intra-abdominal sepsis</td>
<td>43</td>
<td>2</td>
<td>4.17</td>
</tr>
<tr>
<td>Septicemia</td>
<td>43</td>
<td>2</td>
<td>4.17</td>
</tr>
</tbody>
</table>
Reduced number of operating personnel (max 5/table)
Disposable gloving and doing
Scrubbing up for 5 min for first case and 3 min for subsequent cases is ideal
Glove washing before incision to identify the unnoticed holes and wash away the starch powder
Draping of wound whenever suspect contamination
Reoperation through same previous incision
Thorough peritoneal wash and peritoneal drain in contaminated cases
Effective hemostasis, limited sutures, use of more of absorbable than non-absorbable to be employed
Skin closure with subcuticular vicryl/adhesive tapes, especially in elective cases
In contaminated wounds, primary closure with subcutaneous drains with irrigation is ideal
If gross sepsis is suspected entire wound is left unsutured, temporarily covered by dressing or skin closed with loose stitches. After the sepsis controlled wound is closed in layers
Exposure technique helpful to minimize post-operative infection rate
The number of visitors to post-operative wards to restricted and kept clean
Infected cases to be isolated with separate instruments, dressing, and nursing care
A routine culture sensitivity of infected cases including quantitative culture to be done
Laparoscopic procedure whenever necessary will reduce the infection rate.

Finally, the surgeon should adapt a checklist system regarding decision-making, and avoidance of complication is all that requires for achieving good results.

REFERENCES
Visual Outcome in Ocular Injuries in Road Traffic Accident

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Abstract

Introduction: Ocular injuries in Road traffic accidents constitute a major cause of visual morbidity worldwide with significant economic impact.

Aim: The aim of this study to assess the visual outcome in ocular involvement in road traffic accident (RTA).

Methods: Prospective study of RTA cases in a tertiary care hospital to find the visual outcome. Patients were clinically examined, and vision was checked.

Results: Maximum of RTA in 21-30 years, 34.02%, maximum number of ocular injuries happened in two wheeler accidents. 15.27% of patients vision worsened after injury, 37.5% had no change in vision.

Conclusion: Ocular injury as and when occurred has to be tackled urgently and methodically if the final visual outcome is to be improved.

Key words: Injury, Ocular trauma, Road traffic accident, Visual outcome

INTRODUCTION

The eye is the most delicate and highly evolved sense organ contributing 40% sensory inputs to the brain. A trauma which causes little or no concern can cause permanent blindness if it occurs in the eye. There is inordinately high rate of ocular trauma relative to surface area exposed to eye injury. Ocular trauma once described as “neglected disorder” has recently been highlighted as a major cause of visual morbidity.¹ The largest group of causes documented for total ocular trauma group was motor vehicle accident.² In addition to the impact on affected individual, there are profound social implications regarding the lost productivity of young men requirement of caring facilities and rehabilitation for the elderly. Thus, there is a great need for more active interest in the prevention of eye injuries and it is necessary to accumulate relevant data regarding damage caused by road traffic accident (RTA).

Aim

The aim of this study to assess the visual outcome in ocular involvement in RTA.

MATERIALS AND METHODS

This was a prospective study conducted on 144 cases of ocular trauma in RTA attending tertiary care hospital were studied. Institutional Ethics committee and Informed consent from selected patients were obtained. The patients with ocular injury were randomly included in the study. Patients of all ages, both males and females irrespective of economic status, who are co-operative, were included in the study. Patients who were unconscious, not cooperative and terminally ill were excluded. Patients with ocular injuries other than RTA are excluded from the study. Detailed work up was done of the patients with ocular trauma in RTA, which included a detailed trauma history, whenever possible from the patient himself and if necessary from the relatives. History of preexisting ocular and medical trauma
was also recorded. Proforma was drawn up and following details were recorded for each patient with ocular trauma; age and sex, type of vehicle the patient was travelling in, presence or absence of protective eyewear and sign and symptom following the injury.

**RESULTS**

In 144 cases, a maximum number of RTA cases in 21-30 age group 34.02% followed by 43 cases 29.84% in 31-40 age group. Out of 144 patients, 130 patients (90.3%) who sustained ocular injury were males and 14 patients (9.7%) were females.

A maximum incidence of ocular injuries was seen among those travelling by two wheelers, 123 patients (85.4%) sustained injuries while travelling in 2 wheelers, 4 patients (2.8%) in 3 wheelers, 13 patients (9.0%) in 4 wheelers and 4 patients (2.8%) were pedestrians (Table 1).

A total of 130 patients (90.2%) had unilateral involvement and 14 patients (9.72%) had bilateral involvement. In our study, unilateral injuries were seen in 90.3% and bilateral in 9.7%. In the study done by Kriedl et al. (2003), unilateral injuries were seen in 95.1% of patients and bilateral in 4.9% (Table 2).

Out of 144 patients many patients had multiple ocular structure involvement, orbital lesions were seen in 33 patients (22.91%), lids were involved in 117 patients (81.25%), conjunctiva in 92 patients (63.8%), cornea in 13 patients (8.33%), sclera in 5 patients (3.47%), pupil was involved in 31 patients, lens in 6 patients, (4.16%) posterior segment was involved in 15 patients (10.41%), and cranial nerves were involved in 25 patients (17.36%) (Tables 3 and 4).

**DISCUSSION**

This study of 144 patients with ocular injuries following RTA, demonstrates a wide spectrum of serious ocular injuries. In our study, patients <30 years accounted 45.13% of the cases while in the study done by Shtewi et al.4 patients <33 years accounted for 82%. In the study done by Kriedl et al.3 unilateral injuries were seen in 95.1% of patients and bilateral in 4.9%. In our study echymosis was seen in 64.58% of patients, in comparison to the study by Shtewi et al.4 in which it was seen in 37.7%. In our study, lid edema was seen in 65.88% patients while in the study by Shtewi et al.4 and it was seen in 35.5%. 14.58% of patients in our study had lid laceration, while in the study by Shtewi et al.4 and it was seen in 17.8%. Orbital fractures in our study were seen in 22.22% of patients while these accounted to 1.1% in the study by Shtewi et al.4 In a study done by Cruz et al.5 cause of orbital fracture was attributed to RTA in 54% of cases. In our study, 58.33% patients had subconjunctival hemorrhage while in the study by Shtewi et al.4 and 42.4% were found to have the same. Corneal abrasion was seen in 2.77% of patients in our study while in the study by Shtewi et al.4 it was seen in 30.4%. In our study, corneal perforation was seen in 4.86% while in the study by Shtewi et al.4 and it occurred in 46.7%. Hyphema was seen in 4.16% patients in our study while it occurred in 50% cases in the study by Shtewi et al.4 Traumatic cataract occurred in 1.38% in our study and in 31.9% in the study by Shtewi et al.4 Lens dislocation occurred in our study in 2.08% while it occurred in 7.6% cases in the study by Shtewi et al.4 Vitreous hemorrhage was seen in 0.69% of our patients while it occurred in 23.6% of the patients in the study by Shtewi et al.4 In our study, only one patient (0.69%) had IOFB while in the study by Shtewi et al.4 it was seen in

<table>
<thead>
<tr>
<th>Type of vehicle involved in ocular injuries</th>
<th>Number of cases (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 Wheeler</td>
<td>123 (85.4)</td>
</tr>
<tr>
<td>3 Wheeler</td>
<td>17 (11.8)</td>
</tr>
<tr>
<td>4 Wheeler</td>
<td>13 (9.0)</td>
</tr>
<tr>
<td>Pedestrians</td>
<td>4 (2.8)</td>
</tr>
</tbody>
</table>

**Table 2: Eye involved**

<table>
<thead>
<tr>
<th>Eye involved</th>
<th>Number of cases (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unilateral</td>
<td>130 (90.2)</td>
</tr>
<tr>
<td>Bilateral</td>
<td>14 (9.72)</td>
</tr>
</tbody>
</table>

**Table 3: Ocular involvement**

<table>
<thead>
<tr>
<th>Ocular involvement</th>
<th>Number of cases (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Orbital</td>
<td>33 (22.91)</td>
</tr>
<tr>
<td>Lids</td>
<td>117 (81.25)</td>
</tr>
<tr>
<td>Conjunctiva</td>
<td>92 (63.8)</td>
</tr>
<tr>
<td>Cornea</td>
<td>12 (8.33)</td>
</tr>
<tr>
<td>Sclera</td>
<td>5 (3.47)</td>
</tr>
<tr>
<td>Anterior chamber</td>
<td>8 (5.55)</td>
</tr>
<tr>
<td>Pupil</td>
<td>31 (21.52)</td>
</tr>
<tr>
<td>Lens</td>
<td>6 (4.16)</td>
</tr>
<tr>
<td>Posterior segment</td>
<td>15 (10.41)</td>
</tr>
<tr>
<td>Cranial nerves</td>
<td>25 (17.36)</td>
</tr>
</tbody>
</table>

**Table 4: Visual outcome**

<table>
<thead>
<tr>
<th>Ocular involvement</th>
<th>Vision</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Improved</td>
<td>Static</td>
</tr>
<tr>
<td>Anterior segment</td>
<td>68</td>
<td>45</td>
</tr>
<tr>
<td>Posterior segment</td>
<td>9</td>
<td>4</td>
</tr>
<tr>
<td>Cranial nerves</td>
<td>6</td>
<td>5</td>
</tr>
</tbody>
</table>

*Pearson chi-square test
9.8% of patients. In our study, 95.13% of patients had closed globe injury and 4.86% had open globe injury while in a study done by Serrano et al., among boys 82.4% had closed globe injuries and 17.6% had open globe injuries and among girls, 83.8% had close globe injuries and 16.2% had open globe injuries. In another study done by Smith et al. 68.58% of patients had closed globe injury and 31.41% patients had open globe injury. In our study 44.44% patients had visual outcome of 6/6, 39.58% had 6/9-6/60, 5.5% had CF, 3.47% had PL, and 6.24% had no perception of light while in the study by Shtewi et al., 30.43% patients had 6/6, 50.30% patients had 6/9-6/60, 15.94% had CF and 3.28% had no perception of light.

CONCLUSION

Ocular injuries due to RTA involved the lids which while causing a certain degree of cosmetics disfigurement and do not have any effect on any final visual outcome. Only those injuries which involved the globe had a poor prognosis for the final visual outcome.

REFERENCES

Clinical Profile of Ingestional Hair Dye Poisoning: A Prospective Study

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Abstract

Introduction: Ingestional hair dye poisoning is emerging as leading cause of self-harm in households. paraphenylenediamine (PPD) poisoning has protean manifestations, which have been studied here.

Aim: The aim of this study was to evaluate the clinical profile of ingestional hair dye poisoning.

Materials and Methods: A prospective cross-sectional observational study in patients admitted with a history of hair dye ingestion with classical symptoms of neck swelling, muscle pain, and dark-colored urine.

Results: About 82.60% of the patients had angioedema involving the lips, neck, tongue, sublingual structures, and pharynx. 80.43% of patients had discoloration of urine to brownish-black color. Muscle pain, swelling is seen in 80.43% of the individuals.

Conclusion: Early hospitalization, identification, and appropriate treatment ensure good outcome in PPD ingestional poisoning cases.

Key words: Cervicofacial edema, Hair dye poisoning, Mortality, paraphenylenediamine poisoning

INTRODUCTION

The overall suicide rate due to self-poisoning was about 31% in South India.¹ The highest rates of poisoning were due to household agents, drugs, insecticides, chemicals, animal, or reptile bites in the descending order of frequency.² Among the household articles used for self-harm, drugs (prescribed for other medical or surgical conditions for self or for others) and chemicals (lavatory cleaners and hair dye) are noteworthy. Permanent hair coloring is done by the use of oxidation dyes. These are composed of paraphenylenediamine, a coupling agent, and an oxidant. Oxidizing agents are primarily hydrogen peroxide. Coupling agents are usually derivatives of aniline. The mechanism of coloring of hair involves three steps, i.e., oxidation of p-phenylenediamine derivative to the quinine state, reaction of the resultant compound with a coupler, and oxidation of the resulting compound to the final dye.³ The characteristic features of paraphenylenediamine poisoning, namely, rhabdomyolysis and airway edema are characteristically absent in pure propylene glycol poisoning.⁴ In the absence of specific antidote and the relative easy availability of the component, a high index of suspicion, early preventive measures is required for a good outcome. Systemic toxicity may occur due to suicide, accident, or homicide. It is also used as an abortifacient. Skin and eye contact causes skin irritation, contact dermatitis, lacrimation, and chemosis. It may also cause exophthalmos or even permanent blindness due to the local contact. The lethal dose is estimated to be 7-10 g in various studies.⁵

Aim

The aim of this study was to evaluate the clinical profile of ingestional hair dye poisoning.

MATERIALS AND METHODS

A prospective cross-sectional observational study conducted in the Government Rajaji Hospital, Madurai,
Tamil Nadu. The Institutional Ethics Committee approval and informed consent from the patients/relatives were obtained. Patients admitted with a history of hair dye ingestion with classical symptoms of neck swelling, muscle pain, and dark-colored urine were included in the study. Demographic details include age, gender, education, and occupation of the individual. Clinical details include cervicofacial edema, limb pain and swelling, discolored urine, oliguria, dyspnea, palpitation, syncope, voice change, pulse and blood pressure data, and oxygen saturation recorded in the bedside using a finger pulse oximeter. Laboratory data to be collected include urine analysis for protein, deposits; blood total count, blood urea, creatinine, sugar, serum sodium, potassium, serum total creatinine kinase (CPK), serum glutamic oxaloacetic transaminase, serum glutamic pyruvic transaminase, electrocardiogram (ECG), and serum cardiac troponin T for patients, in whom there are ECG changes and/or symptoms and signs of myocarditis such as tachypnea, tachycardia, and hypotension. Treatment details to be collected include airway management requiring tracheostomy or endotracheal intubation, ventilatory support, dosage, duration, and type of steroids used, whether alkaline diuresis used, dialysis details if done, the use of vasopressor, antiarrhythmics, or cardioversion. Cervicofacial edema discolored urine, muscle pain and swelling were noted in the first 24 h of admission. Oliguria, dyspnea, palpitation, syncope, seizures, etc. were taken into consideration when present any time during the hospital stay. Urinalysis, blood urea, creatinine, serum electrolytes, and serum CPK were taken on admission, the 2nd day and periodically once in 1 or 2 days thereafter. The 2nd-3rd day values and discharge day values are taken into consideration for the study. ECG was taken for all patients during admission, and thereafter, only if the patient has persistent tachycardia, electrolyte abnormalities, hypotension, dyspnea, tachypnea, and chest pain. If ECG changes were present, cardiac troponin T was done.

RESULTS

About 52 patients admitted with hair dye ingestional poisoning were included; 46 patients were included in the study.

The majority of the patients were females, comprising almost two-thirds of the cases. In both genders, the 15-35 years age group comprised more than 80% of the total number of patients (Table 1).

About 82.60% of the patients had angioedema involving the lips, neck, tongue, sublingual structures, and pharynx. 80.43% of patients had discoloration of urine to brownish-black color. Muscle pain, swelling is seen in 80.43% of the individuals (Table 2). Proteinuria was found in 20 patients (43.47%); Serum creatinine was elevated in 27 patients (58.69%), out of whom, only 9 patients required dialysis, other 18 patients recovered with fluid management and alkalizing management of urine. Serum CPK levels were elevated in 36 patients (78%), which gradually decreased in the majority of patients with the establishment of normovolemic status with fluids management and forced alkaline diuresis. 6 patients had ECG changes such as tachycardia and non-specific ST/T changes, of which, 1 patient had elevated cardiac troponin. All patients were treated with steroids; out of 38 patients who had edema of the face, neck, tongue, pharynx and only 20 patients required tracheostomy. 2 patients were required mechanical ventilation. 6 out of 46 patients (13.05%) were expired. The duration of hospital stay was directly proportional to the complications and interventions. The average duration of stay was 5-7 days for those who were managed totally conservatively for airway edema, renal failure, etc. For those who had tracheostomy, and without hemodialysis for elevated renal parameters, the duration of stay was 7-10 days. For those who had renal failure and on hemodialysis, 2-3 weeks stay was required to recover from the illness.

DISCUSSION

Since there is no antidote, early recognition of the condition along with institution of early treatment is very important to ensure a good outcome. In our study, 93.4% of individuals consumed the hair dye with an intention of self-harm. Only

<table>
<thead>
<tr>
<th>Table 1: Age distribution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age group (years)</td>
</tr>
<tr>
<td>------------------</td>
</tr>
<tr>
<td>15-25</td>
</tr>
<tr>
<td>26-35</td>
</tr>
<tr>
<td>36-45</td>
</tr>
<tr>
<td>&gt;45</td>
</tr>
<tr>
<td>Total</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Table 2: Clinical profile of study patients n=46</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptoms/sign</td>
</tr>
<tr>
<td>----------------</td>
</tr>
<tr>
<td>Cervicofacial edema</td>
</tr>
<tr>
<td>Muscle pain and/or swelling</td>
</tr>
<tr>
<td>Brown black-colored urine</td>
</tr>
<tr>
<td>Oliguria</td>
</tr>
<tr>
<td>Tachypnea, dyspnea</td>
</tr>
<tr>
<td>Hypotension</td>
</tr>
<tr>
<td>Seizures</td>
</tr>
</tbody>
</table>
a meager percentage consumed it accidentally. This rate was consistent with the findings of Jain et al.\(^6\) (97.84%), in a study comprising a large number of patients in North India. All those who consumed it accidentally recovered since they may have stopped consuming the product on the recognition that they are consuming an unpalatable thing. These patients recovered with conservative measures. Regarding the age group, 15-35 years age group comprised nearly 80% of the total number of patients, which is consistent with the findings of Jain et al.\(^6\) and Kondle et al.\(^7\) The majority of patients were females 66% in our study which is also consistent with the findings of various studies done in India. Cervicofacial edema was present in the majority (80%) of patients in our study which is consistent with the findings of Jain et al.\(^6\) and Kondle et al.\(^7\). Urinary discoloration was present in 80% of patients in our study; it was present in 94% and 47%, respectively, in studies conducted by Kondle et al.\(^7\) and Jain et al.\(^6\), respectively. Oliguria was present in 25% of patients in our study; oliguria was present in 100% cases in the study by Sahay et al.\(^9\) and 25% in Jain et al.\(^6\) study. Serum creatinine was elevated in 58.69% patients in our study. Serum CPK was elevated in 25% in Jain\(^5\) study. Steroids were started for all patients on admission and given for 5 days for those with moderate to severe angioedema. Among the patients who had elevated serum creatinine, only nine (33.33%) of them required dialysis Jain et al.\(^6\) study. The mortality rate was almost similar in males and females in our study (12.5% and 16.67%, respectively). Overall mortality was 13.05% in our study and 22.48% in Jain et al.\(^6\) study; mortality rate was lower among patients who received methyl prednisolone (14.02%) compared to hydrocortisone (27.7%) in that study.

**CONCLUSION**

Hair dye is ubiquitous in households; nowadays, it is a potential mode of self-harm whether intentional or accidental. Patients with cervicofacial edema which is a potentially life threatening complication can be saved by early identification and appropriate treatment. Rhabdomyolysis manifesting as muscle pain and tenderness with subsequent renal failure can be managed effectively with adequate hydration and alkalining the urine. Patients presenting early to the hospital have a good outcome with appropriate treatment.

**REFERENCES**


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Prospective Study of Urinary Bladder Injury

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Abstract

Introduction: Due to a significant increase in road traffic accident bladder injury has become a common entity today. It can occur as either isolated injury or as a component of polytrauma. This is a prospective study of bladder injuries resulting due to different modes, with different types of bladder injuries with varied clinical presentation and management protocols.

Materials and Methods: This study comprises 40 cases having bladder injury with various etiologies from all age groups and either sex. A diagnosis was confirmed in each case and management was individualized.

Results: In this study, age group of 20-40 years is most commonly affected with a male predominance. The most common etiology was found to be road traffic accidents (52.5%) resulting in bladder contusion, intraperitoneal rupture, extraperitoneal rupture, or combined rupture. 85% of patients presented with retention of urine and 87.5% of patients had suprapubic tenderness on examination. Management was individualized according to the type of injury and most patients required operative intervention.

Conclusion: Due to fast life with increasing road traffic accidents, the incidence of bladder injury is on the rise. Proper clinical assessment, prompt, and appropriate initial resuscitation and early confirmed diagnosis by radiological evaluation is important for a successful outcome in these cases.

Key words: Bladder contusion, Extraperitoneal rupture, Intraperitoneal rupture

INTRODUCTION

This is a prospective study of patients having urinary bladder injuries resulting from trauma (blunt or penetrating abdominal injuries) or iatrogenic bladder injuries occurring during various gynecological, gen surgical, urological procedures and instrumentation, who were admitted to our hospital during the 2-year period.

Most of the bladder injuries resulting from road traffic accident require a team approach for the management. The team comprises general surgeon, urologist and orthopedic surgeon, as bladder injuries are often associated with pelvic fracture and urethral rupture. Due to the predominance of bladder injuries, mostly due to road traffic accident which is associated with a high velocity impact are mostly associated with other visceral injuries, thus team approach is most crucial in these cases and management should be decided by priority.

In the case of polytrauma, due to attendant shock and associated life-threatening injuries such as chest trauma, head injury or major visceral injuries, bladder injuries may remain unnoticed. Management of bladder injury differs according to the type of bladder injury. Contusion does not require any operative management, extraperitoneal rupture may be dealt conservatively or by surgery, whereas intraperitoneal bladder rupture requires operative interventions in the most cases.

Aims and Objectives

To study the following parameters
1. Incidence of various etiologies of bladder injuries
2. Incidence of various types of bladder injuries
   - Intraperitoneal
   - Extraperitoneal
   - Mixed
   - Bladder contusion
3. Age-related incidence of bladder injuries
4. Sex-related incidence of bladder injuries

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E-mail: shamsukha.dheeraj@gmail.com
5. Incidence of isolated bladder injuries versus incidence of bladder injuries associated with urethral injuries

6. Incidence of the symptoms

7. Incidence of signs

8. To study the prognosis in case of isolated bladder injury

9. Type of bladder injury, management and prognosis regarding the type of bladder injury

10. Incidence of association of bladder injuries with pelvic fractures

**MATERIALS AND METHODS**

- The study comprises detailed clinical cross-sectional study of 40 cases of bladder injury with various etiologies
- Materials for the clinical study were collected from the cases admitted to our hospital
- The study was conducted during the period between June 2014 to June 2016
- Patients of all the age groups and either sex were selected
- The patients having clinical features of bladder injuries, i.e., hematuria, inability to pass urine, and distension of abdomen (bladder not palpable on per abdomen examination) were subjected to further evaluation
- The investigations done on the cases selected for the study were the following
  - Ultrasonography of the Abdomen and Pelvis
  - X-Ray PBH (Pelvis with both hip joints) A-P view
  - Retrograde urethrogram
  - Retrograde cystogram

Working diagnosis was established in each case and the management was individualized according to the presumed diagnosis.

**OBSERVATIONS**

The total numbers of patients included in this study over a period of 2-year were 40. Patients having evidence of isolated bladder injury, combined bladder, and urethral injury were included in this study.

- Total number of patients studied: 40
- Total death: 01.

A total of 40 patients were admitted over a period of 2-year from June 2014 to June 2016. Among which 9 patients had polytrauma. Out of this, 1 patient died in post-operative period due to septicemia.

**Investigations**

Out of all the patients admitted retrograde urethrogram was done in 34 patients, retrograde cystogram in 19 patients and ultrasound was done in 31 patients.

<table>
<thead>
<tr>
<th>Radiological investigations</th>
<th>Number of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Retrograde cystogram</td>
<td>19</td>
</tr>
<tr>
<td>Retrograde urethrogram</td>
<td>34</td>
</tr>
<tr>
<td>Ultrasound of abdomen and pelvis</td>
<td>31</td>
</tr>
<tr>
<td>Post-operative cystogram (10th day)</td>
<td>15</td>
</tr>
</tbody>
</table>

**Incidence of Signs of Bladder Injury**

The most frequently observed sign was suprapubic tenderness, which was present in 35 patients. The next common was scrotal or perineal swelling present in 21 patients.

Distention of abdomen was present in 15 patients; blood at tip of meatus was present in 13 patients and vulval edema in 3 female patients.

**Management of Bladder Injuries**

Only one patient was treated conservatively. Rest all the patients were managed with operative interpenetrations and the minimum operative intervention done was proximal urinary diversion with suprapubic cystostomy. Patients in whom exploratory laparotomy was required the rent in bladder was sutured in two layers by absorbable suture material (vicryl 2-0). Associated abdominal injury/injuries were dealt accordingly during the laparotomy. Urethral injuries were dealt after 12-36 weeks.

**DISCUSSION**

With the fast modern life, there is sudden increase in road traffic accident and high-velocity trauma hence injury to urinary bladder, urethra with associated pelvic fracture has become quite common.

In this study road, traffic accidents account for the most common etiology of the urinary bladder injury and urethral injuries the incidence being 52.2% which is slightly lower than described by Allen Morey in the study of its 114 patients from 1965 to 1997. Because our set up is located near Mumbai Pune expressway and Mumbai - Goa highway and because of the immense high speed of the vehicles and heavy traffic, road traffic accident was the most common etiology of bladder injury in our hospital. Assault over the abdomen or blow over the abdomen accounted for 15%, fall from height 12.5%, per urethral instrumentation 10%, difficult labor 5%, and gynecological or abdominal surgeries accounted for 5% (Table 1).
Table 1: Etiology of bladder injuries

<table>
<thead>
<tr>
<th>Etiology</th>
<th>Number of patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Road traffic accident</td>
<td>21 (52.5)</td>
</tr>
<tr>
<td>Assault injury over abdomen</td>
<td>6 (15)</td>
</tr>
<tr>
<td>Fall from height</td>
<td>5 (12.5)</td>
</tr>
<tr>
<td>Difficult/prolonged labor</td>
<td>2 (5)</td>
</tr>
<tr>
<td>Surgery (abdominal/pelvic)</td>
<td>2 (5)</td>
</tr>
<tr>
<td>Per urethral instrumentation</td>
<td>4 (10)</td>
</tr>
</tbody>
</table>

Bladder injuries due to prolonged labor were seen in two patients with a history of home delivery conducted without any medical supervision and were referred to us.

<table>
<thead>
<tr>
<th>Injury type</th>
<th>Frequency/1000 procedures</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vaginal delivery</td>
<td>0.1</td>
</tr>
<tr>
<td>Caesarean section</td>
<td>1.8</td>
</tr>
<tr>
<td>Caesarean section</td>
<td>17</td>
</tr>
<tr>
<td>Gynecological surgery (All open)</td>
<td>1.5</td>
</tr>
<tr>
<td>Hysterectomy:</td>
<td></td>
</tr>
<tr>
<td>Vaginal</td>
<td>9</td>
</tr>
<tr>
<td>For radical cancer</td>
<td>14</td>
</tr>
<tr>
<td>Obstetric</td>
<td>61</td>
</tr>
<tr>
<td>Gynecological surgery (All laparoscopic)</td>
<td>3</td>
</tr>
<tr>
<td>Diagnostic</td>
<td>0.1</td>
</tr>
<tr>
<td>Sterilization</td>
<td>0.2</td>
</tr>
<tr>
<td>Hysterectomy (All)</td>
<td>10</td>
</tr>
<tr>
<td>Laparoscopically assisted vaginal</td>
<td></td>
</tr>
<tr>
<td>Hysterectomy</td>
<td>28</td>
</tr>
<tr>
<td>TUR of bladder tumor</td>
<td>25</td>
</tr>
<tr>
<td>(intraperitoneal)</td>
<td></td>
</tr>
<tr>
<td>TURP (Intra/extraperitoneal)</td>
<td>0.1</td>
</tr>
<tr>
<td>Laparoscopic bladder neck suspension</td>
<td>19</td>
</tr>
<tr>
<td>Tension-free vaginal tape for urinary</td>
<td></td>
</tr>
<tr>
<td>Incontinence</td>
<td>0.4</td>
</tr>
<tr>
<td>Laparoscopic hemiorrhaphy</td>
<td>1.6</td>
</tr>
</tbody>
</table>

The frequency (per 1000 procedures) of iatrogenic bladder injuries in published series (55).

In our study, we have not encountered bladder injuries following medical termination of pregnancy. Abdominal hysterectomy for gynecological pathology accounted for 5% of bladder injuries. This was far less than what is reported by Dobrowolski et al. from Poland in their study 49% bladder injury were iatrogenic in nature. The iatrogenic injuries were 39% in urological department, 53% in gynecological department, and 9% in surgical department. No any penetration etiology of bladder injury like gunshot, stab, and missile injuries was present which are more commonly seen during the war or anti-insurgency operations.

There was no case of bladder injury or urethral injury due to an accident in the mining or quarries as described in the literature. Bladder injuries in our study most commonly affected age group was from 21 to 35 years. The maximum incidence in this age group may be attributed to mobility of the people in this age group, 40% of the patients fall into this category which is followed by 37.5% patient in age group 36-50 years in this series, there was no patient with bladder injury in age group ranging from 1 to 10 years.

The incidence of serious lower urinary tract injury in children is lower than that in adults, reported as 0.2% of admissions to a pediatric trauma center. In children with pelvic fracture the incidence was 0.5-3.7% which was also lower than that in adults. Car seat belt injuries have been reported in children who were restrained passenger in motor vehicle crashes. In addition to bladder rupture, lumbar spine and bowel injuries were also seen. These injuries are thought to be a result of poor fitting of the adult seat belt which restrains the child’s abdominal wall and not the anterior superior iliac spine, as intended for the adults.

Bladder rupture in a neonatal period usually presents as urinary ascites. Other reported cases of pediatric bladder injury include child abuse, imperforate hymen, and iatrogenic injury during inguinal hernia repair.

Females accounted for 20% of all cases. This is more than that in the study by division of emergency medicine of Utah where out of 146 patients with fracture of pelvis only 0.7% had bladder rupture and no patient had urethral injury.

Female urethral injury secondary to trauma is rare but has been described in association with pelvic fracture in as many as 6% of cases. Associated urethral injury in women with pelvic fracture is rare because of the short length of urethra, mobility and lack of attachment to pubic symphysis. In our study, the incidence of associated urethral injury was nil. In this the most common symptom suggestive of bladder injury was not able to pass urine since trauma which was present in 85% of the patients. Pain in lower abdomen was present in 65% patients followed by gross hematuria which was observed in 58% of cases (Table 3) This incidence of gross hematuria was less than as mentioned by Corrie and Sandler and Morey and McAnich in their studies, gross hematuria was positive hallmark of a bladder injury accounting over 95% of time. This difference may be attributed to the inclusion of both bladder and urethral injury in the study.

Suprapubic tenderness was the most frequently observed sign in 87.5% of the patients followed by scrotal or perineal swelling seen in 52% of the patients due to extravasation of urine in prevesical space or due to hematoma (Table 4). Distension of the abdomen was present in 37.5% of the patients, mostly seen in intraperitoneal rupture of bladder and in cases of polytrauma; patient having polytrauma...
had associated with hollow viscus or solid organ injury. Distension of the abdomen became more prominent following resuscitation for the hypovolemic shock which may be attributed to sequestration of the fluid in the third space and in the case of intraperitoneal rupture due to collection to urine in the peritoneal cavity following resuscitation due to improved urine output.

Blood at the tip of meatus was observed in 32.5% of the patients. Blood at the tip of meatus is a cardinal sign of posterior urethral injury and is seen in 37-93% of cases. The diagnostic triad of blunt urethral injury is a pelvic fracture, blood at the tip of urethral meatus and inability to void urine. Overall blood at the meatus is the most important sign of urethral injuries - 98% and 75% sensitive for posterior and anterior urethral injuries, respectively. In this study, all urethral injuries were of posterior urethra.

Blood expelled per meatus is a result of spasm of the bulbospongiosus muscle and is often apparent after an hour of injury. The length of urethral injury correlates little with the severity of the injury. Blood at the tip of meatus should preclude attempts of catheterization until urethra is imaged adequately. In the study, blood at the tip of meatus was present in 81% of the urethral injuries.

About 11 patients presented with hypovolemic shock, most of these patients had pelvic fracture and associated injuries like retroperitoneal hematoma and solid organ injuries with associated hemoperitoneum. All the patients were adequately resuscitated.

Bladder injury following history of binge drinking was present in 8 cases, out of them 5 patients had intraperitoneal rupture and 2 had extraperitoneal rupture and 1 had bladder contusion. Out of the 8 patients, in 4 patients’ history of blow over abdomen following binge drinking was present. The more incidence of intraperitoneal rupture can be explained by the full bladder after binge drinking and the trauma causes tear of the bladder at the fundus - the weakest point.

Fracture pelvis was present in 52.5% patients with bladder injuries out of these 48.5% had extraperitoneal rupture of the bladder, 24% had bladder contusion associated with pelvic fracture, combined rupture accounted for 14% of pelvic fracture (Table 5). In all case, the pelvis was fractured at more than one site, i.e., pelvic ring disruption mostly affection pubic rami. Although stated in many reports that the most injuries associated with pelvic fracture occur adjacent to the fracture, this is seen only 35% of the time, in the other 65% cases no relationship exist between the fracture and site of the bladder injury and the injury is commonly opposite to the area of fracture (countercoup injury) implying that a bursting or tearing of the bladder wall is true mechanism rather than the laceration by bone. 86% of the pelvic fracture in this study were treated conservatively and 14% treated by operative intervention.

Dalal et al. reported 95% of the patient with the extraperitoneal rupture of bladder have associated fracture pelvis. In this study, contrast imaging with Urograffin 76% was done. The first imaging study was ultrasonography of abdomen and pelvis done in 31 patients.

Retrograde urethrogram was done before per urethral catheterization in all patients with a history of road traffic accident, fall from height and assault to rule out urethral injuries.

Retrograde static cystogram was performed in 19 patients. Cystogram was performed after injecting 400 ml of diluted contrast via per urethral route and taking the radiographic picture. In this study, the results of an optimally performed cystogram were satisfactory. Imaging of bladder using only excreted contrast material by computed tomography (CT) scan or by conventional radiography is not adequate and results in false negative. On a conventional cystogram, the area behind the bladder should be imaged after the instilled contrast has been drained to obviate missing extravasation obscured by intravesical contrast. When a CT cystogram is performed, this is unnecessary.

Extraperitoneal rupture of the bladder was seen in 40% of the patient in our series. Various published classification of injuries to the urinary bladder exist but at the 2002 consensus panel, four categories and incidence of bladder

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### Table 2: Symptomatology

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Number of patients (%)</th>
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<tbody>
<tr>
<td>Pain in abdomen</td>
<td>25 (63)</td>
</tr>
<tr>
<td>Distention of abdomen</td>
<td>19 (48)</td>
</tr>
<tr>
<td>Pain in hips</td>
<td>22 (55)</td>
</tr>
<tr>
<td>Not passed urine</td>
<td>34 (85)</td>
</tr>
<tr>
<td>Gross hematuria</td>
<td>23 (58)</td>
</tr>
</tbody>
</table>

### Table 3: Incidence of signs

<table>
<thead>
<tr>
<th>Modes</th>
<th>Number of patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Distention of abdomen</td>
<td>15 (37.5)</td>
</tr>
<tr>
<td>Suprapubic tenderness</td>
<td>35 (87.5)</td>
</tr>
<tr>
<td>Guarding</td>
<td>19 (47.5)</td>
</tr>
<tr>
<td>Blood at tip of meatus</td>
<td>13 (32.5)</td>
</tr>
<tr>
<td>Scrotal/perineal swelling</td>
<td>21 (52.5)</td>
</tr>
<tr>
<td>Vulval edema</td>
<td>3 (7.5)</td>
</tr>
</tbody>
</table>
contusion was not exactly defined. The incidence of extraperitoneal rupture was 54-55%, intraperitoneal rupture was 38-40% combined intra- and extra-peritoneum rupture was 5-8% (Table 2).

Incidence of intraperitoneal rupture in our series was 37.5% that corresponds to the incidence reported by 2002 consensus panel. The intraperitoneal bladder rupture is seen in a person who is having full bladder at the time of injury and it is commonly observed in people who are drunk. Combined injuries, i.e., both intra- and extra-peritoneal are observed in 15% of the patients in our study. This incidence is almost double that of reported at 2002 consensus panel.  

Associated urethral injuries were presented in 16 patients, posterior urethral injuries were presented in 9 patients, and only membranous urethral injuries in 7 patients. All these patients with urethral injuries were male female urethral injury secondary to trauma is rare but has been described in association with pelvic fractures in as many as 6% cases. The injury is usually associated with a vaginal laceration which is the most frequent clue in reaching to diagnosis. Labial edema, hematuria, and urethrorrhagia may also be present. Unfortunately, these injuries are frequently missed because a vaginal examination is omitted in severely injured patients. Imaging of female urethra in the case of suspected disruption may be difficult, retrograde urethrography may be difficult, retrograde urethrography is technically challenging in this setting, and may reveal varying degree of contrast extravasation and bladder compression by pelvis hematoma. McAninch has suggested that females with suspected urethral injuries should undergo diagnostic urethroscopy.

All patients with intraperitoneal rupture of the bladder and combined injury, i.e., both intra- and extra-peritoneal rupture without urethral rupture were treated by the closure of the rent in two layers, water tight closure by absorbable suture materials. In all our patients’ suprapubic diversion of urine was done after closure of rent or rents using a large bore Foley’s catheter besides placement of per urethral Foley’s catheter. Ali and Mohammad Ozair et al. in the prospective study evaluated combined suprapubic and urethral catheterization to urethral drainage alone for intraperitoneal injuries and concluded that urethral catheterization is adequate to effect the drainage after intraperitoneal bladder injury. In addition, it is associated with a shorter hospital stay and lower morbidity.

In our study, only one case of extraperitoneal rupture was treated conservatively, i.e. with periurethral drainage and broad spectrum antibiotics. Rest all the patients were treated by water tight closer of rent or rents in two layers using absorbable material with suprapubic urinary diversion.

Concomitant urethral injury in this study was not treated primarily. The policy of deferred treatment was adopted, i.e., treatment 3 months after injury.

Primary suturing of the severed urethral ends, although once commonly performed has been abandoned because of high rates of post-operative impotence and incontinence, at 56% and 21%, respectively, in a literature meta-analysis compared with a deferred treatment approach stricture is less common at 49% but impotence and incontinence are three times and five times worse, respectively. Other problems with primary suturing were the potential release of pelvic hematoma tamponade (risking uncontrolled bleeding) excessive urethral debridement and subsequent stricture (technically demanding) and the possibility of converting an incomplete to complete urethral injury during dissection.

The major advantage to the deferred treatment is that in exchange for a high posterior urethral stricture rate is low reported incidence of long-term impotence or incontinence. In meta-analysis by Koritim, the overall complication rate of deferred treatment of posterior urethral injuries are posterior urethral stricture (97%) impotence (19%) and incontinence (4%).

In sharp contrast to the management of male urethral injuries, women with pelvic fractures and proximal urethral disruptions are recommended to undergo immediate retropubic exploration with the realignment of the urethral ends are primary anastomosis over catheter.  

In our study, out of 16 patients of urethral injury, one patient developed recurrent stricture of urethra requiring frequent dilatation cystoscopically. One patient develops both impotence and incontinence. Periurethral abscess and fistula were noted on one patient.

### Table 4: Association of pelvic fracture

<table>
<thead>
<tr>
<th>Pelvic fracture</th>
<th>% of PT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Present</td>
<td>52.5</td>
</tr>
<tr>
<td>Absent</td>
<td>47.5</td>
</tr>
</tbody>
</table>

### Table 5: Type of bladder injuries

<table>
<thead>
<tr>
<th>Modes</th>
<th>Number of patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intraperitoneal rupture</td>
<td>15 (37.5)</td>
</tr>
<tr>
<td>Extraperitoneal rupture</td>
<td>16 (40)</td>
</tr>
<tr>
<td>Combined</td>
<td>6 (15)</td>
</tr>
<tr>
<td>Bladder contusion</td>
<td>3 (7.5)</td>
</tr>
</tbody>
</table>


The most common complication was lower urinary tract infection evident in 27.5%. This is similar to that of retrospective analysis of traumatic bladder injury by Daniel et al. in which they reported 28% incidence of urinary infection when both suprapubic and urethral drainage were employed as compared to 19% incidence when transurethral drainage alone was employed. In most cases organisms isolated were E. coli, Pseudomonas aeruginosa, Klebsiella and yeast. The increased incidence of urinary infection may be attributed to our policy of suprapubic diversion. Alli et al. in a prospective study of combined suprapubic and urethral catheterization to urethral drainage alone have reported, increased incidence of urinary tract infection with former that when urethral drainage alone is employed.

Other complications like bilateral foot drop were observed in one female patient following orthopedic treatment for pelvic fracture. Foot drop was treated by conservative means. Hematemesis and melena was observed in one patient on tenth post-operative day. Oesophagogastroduodenoscopy was done, which shows evidence of erosive gastritis. One patient presented with urinary ascites due to intraperitoneal rupture of bladder who presented to us 24 h after the trauma. Would dehiscence was present in two cases treated by secondary suturing after control of infection (Table 6).

The surgeries for non-urological injuries were performed as follows:

<table>
<thead>
<tr>
<th>Complications</th>
<th>Number of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdominal surgery</td>
<td>5 patients</td>
</tr>
<tr>
<td>Orthopedic surgery</td>
<td>5 patients</td>
</tr>
<tr>
<td>Thoracic surgery</td>
<td>1 patient</td>
</tr>
<tr>
<td>Craniotomy</td>
<td>1 patient</td>
</tr>
</tbody>
</table>

The retroperitoneal hematoma was present in 27 cases and was left undisturbed during surgery in all cases.

**CONCLUSION**

The mortality with lower urinary tract injuries has reduced significantly however the morbidity following these injuries is still high. There is changing trend in the etiology of these injuries. Previously these injuries were more due to trauma sustained during mining, quarrying and war, but nowadays, road traffic accidents and iatrogenic injuries are the major contributor for these injuries. In our study, the road traffic accident was the main etiology which is similar to other studies. This scenario warrants taking appropriate measures to improve road safety like mass education, improving roads conditions, and traffic law enforcement religiously. Again males are a more vulnerable that females and the young persons are more prone for these injuries due to their greater mobility. Males are more prone for composite injury, i.e., bladder and urethral injury. This is the price males have to pay for long urethra. Because of this, morbidity due to these injuries is very high in males. Bladder rupture is not a dreaded injury today if it is treated promptly with the standard protocol as compared to the mortality of 44%, 1942. Proper assessment of the patient clinically and radiologically and appropriate initial resuscitation is important for successful outcome in these cases. Bladder contusion can be managed effectively conservatively while bladder rupture is managed by suturing in two layers with decompression by suprapubic cystostomy. A suprapubic cystostomy is done for all urethral injuries as initial management. The policy of deferred treatment is adopted in the management of urethral injury to minimize the complications like impotence and incontinence. The policy of urethral catheterization is adopted when the urethral injury is ruled out by ascending urethrogram. All should work in a holistic approach to decrease the morbidity associated with these injuries. The policy of adopting good surgical techniques, giving tissue respect, meticulous dissection, and appropriate use of instruments will reduce the incidence of iatrogenic bladder injuries. Anticipating and detecting bladder injuries intraoperatively by constant active vigilance will result into prompt treatment with favorable outcome.

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8. Perry MO, Husmann DA. Urethral injuries in female subject following


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Correlation between Ejection Fraction and Hepatic and Renal Functions in Heart Failure Patients

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INTRODUCTION

Heart failure is a systemic clinical syndrome with a wide range of potential effects on all organ systems in our body like liver and kidney. Specific effects of heart failure on the different body organs depend on whether it occurs on the right or left side. After sometime, in either form of heart failure, the organs in the body will receive more oxygen supply, nutrients or body wastes are removed slowly due to poor cardiac output. Adequate blood supply is necessary for the liver to perform its various functions. As a result of high level of metabolic activity and its complex vascular supply, the liver is particularly vulnerable to a wide spectrum of circulatory disturbances. Heart failure causes a number of pathophysiologica effects alone or in combination, resulting in liver damage. Congestive heart failure causes liver damage in 20% of patients and clinically evident to jaundice. Jaundice correlates with the severity of heart failure as evidenced by pulmonary wedge pressure, right atrial pressure, and cardiac index. However, hyperbilirubinemia is seen in 20-80% of patients with congestive heart failure. The raised serum bilirubin falls quickly with the improvement of heart failure usually becoming normal within 3-7 days. Serum bilirubin level mostly <3 mg/dl and it rarely rises more than 5 mg/dl. Extreme elevation of serum aminotransferases and serum bilirubin would suggest extensive hepatic necrosis. Mild renal dysfunction is a common in heart failure patients. It is intimately associated with heart failure even in its earliest stage. Seattle heart failure model uses serum creatinine as a measure of renal function. Worsening of renal function mainly due to chronic venous congestion, hypoperfusion, or increased intra-abdominal pressure (≥8 mm Hg). In heart failure cases, liver and renal dysfunctions are usually mild and asymptomatic. It is often detected incidentally on routine biochemical investigations. This study was...
undertaken particularly to emphasize the importance of early identification of liver and renal biochemical markers in heart failure patients. The renal and liver function tests are found to be a very useful in assessing the severity and duration of heart failure. Early identification and adequate treatment of the underlying cause of heart failure revert renal and liver derangements to normal and prevents permanent damage.

**Aim**

To study the parallelism between degree of heart failure and impairment of liver and renal functions in heart failure patients.

**MATERIALS AND METHODS**

A prospective cross-sectional study was conducted in tertiary care medical college hospital. Ethics committee approval and informed consent from the patients recruited were obtained. Cases of congestive cardiac failure, as per Framingham criteria, of various age groups and etiologies such as rheumatic valvular heart disease, ischemic heart disease, hypertensive heart disease, congenital heart disease, cardiomyopathies, cor pulmonale, congestive cardiac failure of varied presentation either acute or chronic. Patients with a past history of jaundice, presence of hepatitis B surface antigen and anti-hepatitis C virus antibody, history of alcoholism, pregnancy, recent intake of cholestatic or hepatotoxic drugs, hemolytic disorders, blood transfusion, and infectious hepatitis were excluded from the study. Clinical diagnosis of congestive heart failure was made in patients who met with the inclusion and exclusion criteria. Patient's completed demographic details with complete history were recorded. After hemodynamic stabilization, they were subjected to complete biochemical investigations such as plasma glucose, blood urea, serum creatinine, serum electrolytes, complete hemogram, liver function tests, urine analysis, x-ray chest, ultrasonography abdomen, electrocardiogram, and echocardiography.

**RESULTS**

A total of 100 patients with congestive heart failure fulfilling the inclusion criteria were included in the study. In this study, among 100 total cases, 59 male and 41 female cases were present. The number of male cases was higher than female cases. The higher frequency of cases was found within the age group of <40 years followed by 50-60 years of age group (Table 1).

This study revealed that among the total heart failure patients, 20% cases were dilated cardiomyopathies, 32% cases were rheumatic heart disease, 28% cases were coronary artery heart disease, 12% cases were cor pulmonale. Heart failure secondary to congenital heart disease is seen in 3% of cases. We have found 12 cases with acute heart failure and 5 cases with hypotension.

In patients with ejection fraction ≤40-85% had increased bilirubin, 92.5% had increased serum glutamic oxaloacetic transaminase (SGOT), 92.5% had increased serum glutamic pyruvic transaminase (SGPT), and 22.5% had increased alkaline phosphatase (ALP). In patients with ejection fraction, more than 40-35% had increase bilirubin, 71.7% had increased SGOT, 61.7% had increased SGPT, and 5% had increased ALP.

Ejection fraction did not correlate well with a serum protein, albumin, prothrombin time or liver size in our study (Table 3).

In patients with ejection fraction ≤40-57.5% had increased urea and 62.5% had increased creatinine. In patients with ejection fraction, more than 40-15% had increase urea and 16.7% had increased creatinine (Table 4).

**DISCUSSION**

Serum hyperbilirubinemia is seen in 55% of heart failure patients in our study. Serum bilirubin level ranges

<table>
<thead>
<tr>
<th>Table 1: Age distribution of study patients</th>
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<tbody>
<tr>
<td>Age</td>
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<tr>
<td>----------------</td>
</tr>
<tr>
<td>&lt;40</td>
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<tr>
<td>40-50</td>
</tr>
<tr>
<td>50-60</td>
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<tr>
<td>More than 60</td>
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<tr>
<td>Total</td>
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<table>
<thead>
<tr>
<th>Table 2: Influence of ejection fraction on liver function test</th>
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</thead>
<tbody>
<tr>
<td>Liver function test</td>
</tr>
<tr>
<td>--------------------</td>
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<tr>
<td></td>
</tr>
<tr>
<td>Increased bilirubin</td>
</tr>
<tr>
<td>Increased SGOT</td>
</tr>
<tr>
<td>Increased SGPT</td>
</tr>
<tr>
<td>Increased ALP</td>
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</tbody>
</table>

SGOT: Serum glutamic oxaloacetic transaminase, SGPT: Serum glutamic pyruvic transaminase, ALP: Alkaline phosphatase

<table>
<thead>
<tr>
<th>Table 3: Influence of ejection fraction on liver parameters</th>
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<tbody>
<tr>
<td>Other liver parameters</td>
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<tr>
<td>------------------------</td>
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<tr>
<td></td>
</tr>
<tr>
<td>Decreased serum proteins</td>
</tr>
<tr>
<td>Decreased serum albumin</td>
</tr>
<tr>
<td>Prolonged prothrombin time</td>
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</table>
Table 4: Influence of ejection fraction on renal function test

<table>
<thead>
<tr>
<th>Renal function tests</th>
<th>Ejection fraction</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>≤ 40% (n=40)</td>
<td>&gt;40% (n=60)</td>
</tr>
<tr>
<td>Increased urea</td>
<td>23</td>
<td>9</td>
</tr>
<tr>
<td>Increased creatinine</td>
<td>25</td>
<td>10</td>
</tr>
</tbody>
</table>

between 0.78 and 3.9 mg/dl. Kubo et al. study shows the elevation of serum bilirubin level up to 2.5 mg/dl 20. Dunn et al. found mild elevation of serum bilirubin in 70% of heart failure patients. Shovman et al. described ischemic hepatitis resulting from the acute onset of hypoxia in patients with poor EF. This study also found elevated serum bilirubin level in patients with DCM and hypotension. The serum bilirubin level raises 3-4 folds the normal in ischemic hepatitis. In our study, more than 3-fold rise in serum bilirubin seen with DCM patients. This study shows hepatomegaly in 74% of cases. Liver size ranges from 11 cm to 19 cm. Dunn et al. study shows 95% of hepatomegaly in heart failure patients. Giallourakis et al. study found aminotransferase elevation is usually 2-3 times above the normal range in congestive heart failure. Degree of AT elevation correlates with hypotension and decrease hepatic perfusion. This study shows 80% cases are associated with elevated SGOT 74% mostly the patients with reduce LV function shows the elevation of SGOT and SGPT levels which is highly significant (P < 0.0001). Our study reveals a significant correlation between SGPT and SGOT in heart failure patients. Richman et al. found both SGOT and SGPT were elevated in his study with reference to particular serum enzymes. In this study, SGOT elevated in 80% and SGPT elevated in 74% mostly the patients with reduce LV function shows the elevation of SGOT and SGPT levels which is highly significant (Table 2). The SGOT/SGPT ratio is 1.2 in this study. This study revealed elevation of ALP in 12% cases among 100 heart failure cases. ALP ranges between 26 and 75 Sherlock et al. and Kubo et al. found increased serum alkaline phosphatase by 10-20% cases with heart failure. Richman et al. found high intrahepatic pressure may cause intrahepatic biliary obstruction leads to rise in ALP with congestive heart failure cases. Our study revealed low serum proteins were found in 40% of cases, and low albumin values were found in 44% of cases among 100 heart failure patients. This study found low albumin/globulin ratio in 75% of cases. Naresh et al. found decreased serum albumin level in 39% of cases with heart failure. This study found low serum albumin level in half of the patients. This low serum albumin level should be interpreted with caution because low albumin values were associated with reduced dietary intake of proteins, increased gastrointestinal loss or renal loss, altered vascular permeability, increased catabolism and over hydration. So changes in serum albumin level are not specific for liver disease. Our study revealed prolonged prothrombin time in 76% of cases among 100 heart failure patients, which is considered to be significant. White et al. observed prolonged PT in 80% of cases with acute and chronic heart failure. Giallourakis et al., 2002, study shows PT prolongation in 80% of cases with congestive heart failure. This is due to decreased synthesis of clotting factors II, V, VII, IX and X by liver. Forman et al., 2004, study found 27% cases associated with renal dysfunction. The renal dysfunction defined as elevated creatinine which correlates with left ventricular systolic function. Blood urea elevation is seen in 19.4% of patients. He found worsening of renal dysfunction in patients with reduced left ventricular ejection fraction (LVEF). In our study also worsening of renal function present in 1/3rd of patients. Rusinaru et al. found renal dysfunction in 14% of cases with heart failure patients (LVEF more than or equal to 50). He described renal dysfunction due to heart failure is caused by intrinsic nephropathy, poor renal perfusion, vasoconstriction, and renal venous congestion.

CONCLUSION

The incidence of liver and renal involvement increased considerably with the degree of heart failure. An early and prompt treatment of heart failure is necessary to prevent added morbidities caused by liver and renal involvement. Hence, the liver and renal function tests are warranted for congestive heart failure patients.

REFERENCES


“Comparative Evaluation of Intrathecal Neostigmine with Intrathecal Fentanyl for Post-operative Pain Relief”

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Abstract

Background: Anticholinesterases increase the concentration of acetylcholine at the postsynaptic sites which cause prolonged analgesia. 
Aims Objectives: To evaluate and compare the effects of intrathecal neostigmine and intrathecal fentanyl on post-operative pain relief. 
Materials and Methods: After informed consent, 60 female patients of age between 40 and 60 years, belonging to ASA Grades 1 and 2, posted for TAH under spinal anesthesia were included in the study and randomly divided into 2 groups of 30 each. Patients of Group 1 received intrathecal injection of bupivacaine 0.5% 15 mg (3 ml) with 5 µg neostigmine, and Group 2 received intrathecal injection of bupivacaine 0.5% 15 mg (3 ml) with 25 µg fentanyl.
Results: The mean duration of analgesia in Groups 1 and 2 was 594.67±95.18 min and 309.67±44.91 min, respectively. It was observed that duration of analgesia in Group 1 was longer and statistical significant in comparison to Group 2.
Conclusion: Intrathecal neostigmine provides prolonged post-operative analgesia than intrathecal fantanyl with less side effect and better hemodynamic stability.

Key words: Bupivacaine, Fentanyl, Neostigmine, Total abdominal hysterectomy

INTRODUCTION

A lot of survey over a long time show that many patients still suffer from moderate to severe post-operative pain. There are various methods used for post-operative pain relief, i.e., infiltration of wound with local anesthetics, central neural blockade with adjuvants, and intravenous opioids.

Today regional analgesic technique play an important role in post-operative control of pain, either intrathecally or epidurally, local anesthetic with opioids (morphine, fentanyl, sufentanil, etc.), neostigmine, clonidine, dexmedetomidine, and midazolam, etc. However, use of these adjuvants is not free from their side effects such as respiratory depression, pruritus, urinary retention, sedation, nausea, and vomiting.

Intrathecally neostigmine inhibits the activity of both true and pseudocholinesterases and thereby enhancing acetylcholine at various cholinergic sites which have been shown to cause analgesia. This synaptically released acetylcholine act on muscarinic and nicotinic site on dorsal horn of spinal cord. In post-operative period, descending noradrenergic or cholinergic antinociceptive spinal system is activated by ongoing pain causing an increase in release of acetylcholine, which in the presence of neostigmine results in augmented analgesia.

Opioids analgesics are the cornerstone for the treatment of post-operative pain; these agents generally exert their
analgesic effects through micro receptors in the central nervous system (CNS). Receptor activation leads to G protein-mediated potassium channel opening (µ and Δ) and calcium channel closure (kappa), with an overall reduction in intracellular calcium. This reduces the release of excitatory transmitter (glutamate and substance P) from presynaptic C fibers but not from A fiber terminals with consequent reduction in nociceptive transmission.

**Aim and Objective**

1. To study and compare the effect of intrathecal neostigmine and intrathecal fentanyl on post-operative analgesia
2. To study and compare the side effects.

**MATERIALS AND METHODS**

This is a randomized, prospective study was carried out in the Department of Anaesthesia Shyam Shah Medical College, Rewa, Madhya Pradesh. After informed consent from each of the patient, 60 female patients of ASA Grades I and II, between age groups 40-60 years, weight 45-60 kg and posted for total abdominal hysterectomy under spinal anesthesia were included in the study and randomly divided into 2 groups of 30 each.

**Group 1:** Injection bupivacaine hydrochloride heavy 0.5% 15 mg (3 ml) intrathecal.
Injection neostigmine 5 µg (1 ml) intrathecal.

**Group 2:** Injection bupivacaine hydrochloride heavy 0.5% 15 mg (3 ml) intrathecal.
Injection fentanyl 25 µg (1 ml) intrathecal.

Patients having systemic cardiovascular, respiratory, hepatic, renal or CNS disorders, hemorrhagic disorders, deformities of the spinal cord or vertebral column, and any other contraindication for spinal anesthesia have been excluded from this study.

Preanesthetic examination was done a day before surgery. All the patients were kept nil by mouth for at least 6 h. All patients were preloaded with 15 ml/kg ringer lactate’s solution. Baselines HR, systolic blood pressure, diastolic blood pressure, and SPO\textsubscript{2} were recorded.

Under all aseptic precautions, lumber puncture was performed through midline approach in sitting position between L2-L4 intervertebral spaces using 25 G Quincke’s spinal needle. After the free flow of cerebrospinal fluid, injection bupivacaine with neostigmine injected in Group 1 and bupivacaine with fentanyl in Group 2.

Level of sensory blockade was assessed using a 23 G hypodermic needle. Duration of effective analgesia was measured as time from intrathecal drug administration to the patient’s first complain of pain.

Then, level of motor blockade was assessed by modified Bromage scale (Table 1). Duration of motor blockade was recorded as time from onset of motor block to the time when the patient was able to raise his limb.

Following that subarachnoid block heart rate, systolic blood pressure, diastolic blood pressure, and SPO\textsubscript{2} were recorded at different time intervals. Side effects, i.e., hypotension, nausea, vomiting, desaturation or hypoxemia (SPO\textsubscript{2} <90%), and any others were also recorded. Bradycardia (heart rate <60/min) treated with injection atropine 0.6 mg intravenous (IV); hypotension (fall of systolic blood pressure >20% OR systolic blood pressure <90 mm hg) was treated with IV fluids and/or injection mephentermine 3 mg IV; respiratory depression (respiratory rate <10 or SPO\textsubscript{2} <90%) was recorded and treated by oxygen by face mask.

Pain was assessed by visual analog scale score from “0” as no pain to “100” as worst possible pain at 2, 4, and 24 h after operation.

The data were tabulated and analyzed by student’s t-test and Chi-square test. \( P < 0.05 \) was taken as statistically significant. All were analyzed using SPSS software 11.5.

**RESULTS**

All groups were demographically similar (\( P > 0.05 \)) in regards to age, weight, heights, and duration of surgery, and it can be presumed that the group was comparable for the purpose of the study (Table 2).

All patients in each group have achieved sensory block up to T6 dermatome and complete motor block (Bromage scale Grade 3) (Table 3).

**Table 1: Modified bromage scale**

<table>
<thead>
<tr>
<th>Level</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>No paralysis</td>
</tr>
<tr>
<td>2</td>
<td>Inability to lift outstretched leg</td>
</tr>
<tr>
<td>3</td>
<td>Inability to flex the knee</td>
</tr>
<tr>
<td>4</td>
<td>Total paralysis of lower limb</td>
</tr>
</tbody>
</table>

**Table 2: Patient’s characteristics**

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Group 1</th>
<th>Group 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age in years (mean±SD)</td>
<td>45.20±7.71</td>
<td>43.03±7.87</td>
</tr>
<tr>
<td>Weight in kg (mean±SD)</td>
<td>55.67±4.21</td>
<td>55.17±6.22</td>
</tr>
<tr>
<td>Height in cm (mean±SD)</td>
<td>153.93±4.03</td>
<td>153.77±3.40</td>
</tr>
<tr>
<td>Duration of surgery in minutes</td>
<td>106.33±12.994</td>
<td>107.87±10.954</td>
</tr>
</tbody>
</table>

SD: Standard deviation
The mean onset of sensory block in Groups 1 and 2 was 246.57±95.56 s and 263.97±50.92 s, respectively. This onset of sensory block was comparable in Groups 1 and 2 (Table 3).

The mean onset of motor block in Groups 1 and 2 was 533.90±112.10 s and 553.83±47.12 s, respectively. It was comparable in both the groups (Table 3).

The mean duration of analgesia in Groups 1 and 2 was 594.67±95.18 min and 309.67±44.91 min, respectively. It was observed that duration of analgesia in Group 1 was longer and statistically significant in comparison to Group 2 (Table 3).

The mean of heart rate and systolic and diastolic blood pressure was comparable in both groups and was found to be insignificant.

The most common side effects found in our study were hypotension, bradycardia, nausea, vomiting, shivering, pruritus, and respiratory depression. Mild hypotension was found in 2 patients of Group 1 and 7 patients of Group 2 it was easily corrected with crystalloid infusion and 6 mg IV mephentermine. Bradycardia observed in 1 patient in Group 1 and 4 patients in Group 2 and corrected with IV atropine 0.6 mg. Complained of nausea was in 3 patients of Group 1 and 1 patient of Group 2. Vomiting was in 2 patient of Group 1 and not in any patients of Group 2. Other side effects were minimal, i.e., pruritus and shivering (Table 4).

**DISCUSSION**

Total abdominal hysterectomies associated with moderate to severe pain, thus it may delay recovery and return to daily living. It can cause unsatisfaction of patients with their anesthesia and surgical experiences.

Intrathecal neostigmine provides post-operative analgesia; it was first described by Naguib and Yaksh. Neostigmine has several advantages such as easily available, cost-effective, reliable, and durable post-operative analgesia and also no untoward side effects such as respiratory depression, pruritus, and drowsiness as expressed with intrathecal opioids. Although it was used in different dose ranges from 5 µg to 750 mg by intrathecally. With higher doses (>150 µg), it has more pronounced side effects such as nausea and vomiting, but in our study, we used only 5 µg to alleviate these side effects.

In our study, intrathecal neostigmine cause prolonged duration of analgesia up to 12 h then intrathecal fentanyl, this support the finding of Lauretti et al. and Garg et al. In our study, intrathecal neostigmine increases the time of first rescue analgesia, reported by Lauretti et al. and Pan and Mok in their study. It decreases the requirement of other analgesics and provides longer post-operative analgesia as compared to intrathecal fentanyl (Sergio D Belzarna), and this correlates with the finding of Lauretti et al., Seldasen et al., Fareed Ahmed et al., and Mohammed Algohary.

The rostral spread of neostigmine to the brainstem has contributed to the severity of the side effects such as nausea and vomiting as shown by Hood et al. It was the common side effect of neostigmine, which limits its use but with lower dose and premedication with antiemetics, it can be easily controlled.

Incidence of hypotension and bradycardia was less with neostigmine then fentanyl suggested the more hemodynamic stable property of neostigmine as reported by Carp et al. and Pan and Mok. Shivering, pruritus, and respiratory depression mostly occurred with intrathecal fentanyl were not reported with neostigmine also possessing it more superiority than fentanyl.

It has been proved that intrathecal neostigmine with very low dose can be used to provide post-operative analgesia without distressing adverse effects such as severe nausea, vomiting, and evacuation of bowel and bladder.

**CONCLUSION**

From this study, it was concluded that intrathecal neostigmine provides longer post-operative analgesia
than intrathecal fentanyl, with less side effect and better hemodynamic stability.

REFERENCES


Source of Support: Nil, Conflict of Interest: None declared.
Respiratory Infections and CD-4 Counts in Human Immunodeficiency Virus-seropositive Cases: A Study from Tertiary Care Institute

Sandeep Jain¹, Ashish Sharma²

¹Assistant Professor, Department of Medicine, RD Gardi Medical College, Ujjain, Madhya Pradesh, India, ²Professor, Department of Medicine, RD Gardi Medical College, Ujjain, Madhya Pradesh, India

Abstract

Introduction: Pulmonary disease is one of the most frequent infections in human immunodeficiency virus (HIV)-positive patients. Among them, the protozoal, viral, bacterial infections and tumors such as Kaposi’s sarcoma and lymphoma involving lung often require indoor treatment in hospital. CD4 cell count is an excellent indicator of an HIV-infected patient’s risk of developing opportunistic pulmonary infections presumably because it reflects the stage of HIV disease and degree of immune compromise.

Material and Methods: A total of 50 cases of HIV-infected patients showing clinical evidence of respiratory system involvement and admitted in a tertiary care center in Ujjain, from July 2010 to October 2013 were studied in the present study. Detailed clinical history was noted in each patient with special emphasis on history of major surgery, blood transfusion, genital ulcer, multiple sexual partners, occupational exposure, drug abuse history of tuberculosis, and AKT whether taken or not, history of antiretroviral drugs taken or not and history of pneumonia.

Results: In the present study, the most common opportunistic infection (OI) was pulmonary tuberculosis 33 (66%) followed by bacterial pneumonia 12 (24%) and others were pneumocystis pneumonia 4 (8%), fungal infection seen in 1 (2%) of the cases.

Conclusion: CD4 count is a sign of decreased immunity and higher chances of OIs. HIV and tuberculosis co-infection is a major problem in India. Early diagnosis of HIV infection and initiation of antiretroviral therapy can be helpful in preventing the patients from OIs.

Key words: CD4 cell count, Human immunodeficiency virus, Opportunistic infections, Tuberculosis

INTRODUCTION

Acquired immunodeficiency syndrome (AIDS) is caused by human immunodeficiency virus (HIV). HIV infection is a global pandemic, with cases reported from virtually every country.¹ The spectrum of HIV-related respiratory diseases has evolved since initial years of the epidemic.² People with advanced HIV are vulnerable to infections called “opportunistic infections” (OIs) because organisms take advantage of the opportunity offered by a weakened immune system. Since the beginning of the HIV epidemic, OIs have been recognized as common complications of HIV infection.³⁴

Pulmonary disease is one of the most frequent infections in HIV positive patients. Among them, the protozoal, viral, bacterial infections and tumors such as Kaposi’s sarcoma and lymphoma involving lung often require indoor treatment in hospital. CD4 cell count is an excellent indicator of an HIV-infected patient’s risk of developing opportunistic pulmonary infections presumably because it reflects stage of HIV disease and degree of immune compromise.⁶

Early in the epidemic, Pneumocystis carinii pneumonia was considered the predominant pulmonary disorder. However, epidemiologic shifts and advances in treatment have broadened our perspective on the diseases that patients with HIV infection develop.
*P. carinii* pneumonia has long been considered the predominant pulmonary disease in patients with HIV, but several factors are changing this perception. The population infected with HIV is increasingly composed of injection drug users and racial and ethnic minorities, which represent groups that have a high incidence of bacterial pneumonia and tuberculosis.  

This study was carried out with the aim to study the correlation between CD4 count and respiratory tract infections among HIV-seropositive individuals.

**MATERIALS AND METHODS**

It was a cross-sectional study. 50 cases of HIV-infected patients showing clinical evidence of respiratory system involvement and admitted to a tertiary care center in Ujjain, from July 2010 to October 2013 were studied in the present study.

Detailed clinical history was noted in each patient with special emphasis on history of major surgery, blood transfusion, genital ulcer, multiple sexual partners, occupational exposure, drug abuse history of tuberculosis, and AKT whether taken or not, history of antiretroviral drugs taken or not and history of pneumonia.

Detailed physical examination was carried out in all patients looking, especially for the presence of associated OIs in other systems.

Routine hematological and biochemical, bacteriological, and radiological tests (X-Ray Chest, USG thorax) along with HIV enzyme-linked immunoassayand CD4, CD8 cell count, Hepatitis B surface antigen, and venereal disease research laboratory were carried out in all patients. Special investigation, such as serum lactic dehydrogenase, body fluid examination, and computed tomography (thorax), were performed in patients depending on indication and affordability of patient.

All the patients were treated accordingly in the form of antibiotics, AKT, antiretroviral, and supportive therapy. Prophylaxis for various OIs was given where indicated.

**RESULTS**

In the present study, total number of male patients is 41 (82%) and females are 9 (18%). Out of total 50 patients, 17 (34%) cases were in the age group of 15-29 years, 31 (62%) cases were in the age group of 30-49 years, and 1 (2%) case was in the age group of more than 50 years (Table 1).

In the present study, out of total 50 cases, 23 (46%) cases had CD4 cell count between 200 and 500, which was followed by 16 (32%) cases between 50-199 and minimum 11 (22%) of the cases had CD4 cell count <50 (Table 2).

In the present study, maximum patients 35 (70%) had heterosexual route of transmission. No patient in the present study had homosexual or intravenous route of transmission.

In the present study, fever was the most common presenting symptom in 44 (88%) of the cases followed by cough which was present in 32 (64%) of the cases. Productive cough was present in 24 (48%) of the cases, whereas dry cough was present in 8 (16%) of the cases. Dyspnea was present in 16 (32%) of the cases; chest pain was present in 6 (12%) cases, and hemoptysis was present in 4 (8%) of the cases (Table 3).

In the present study, the most common OI was pulmonary tuberculosis 33 (66%) followed by bacterial pneumonia 12 (24%) and others were pneumocystis pneumonia

<table>
<thead>
<tr>
<th>Age group in years</th>
<th>Male n (%)</th>
<th>Female n (%)</th>
<th>Total n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-14</td>
<td>00 (00)</td>
<td>00 (00)</td>
<td>00 (00)</td>
</tr>
<tr>
<td>15-29</td>
<td>14 (28)</td>
<td>03 (06)</td>
<td>17 (34)</td>
</tr>
<tr>
<td>30-49</td>
<td>26 (52)</td>
<td>05 (10)</td>
<td>31 (62)</td>
</tr>
<tr>
<td>&gt;50</td>
<td>01 (02)</td>
<td>01 (02)</td>
<td>02 (04)</td>
</tr>
<tr>
<td>Total</td>
<td>41 (82)</td>
<td>09 (18)</td>
<td>50 (100)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>CD4 cell count</th>
<th>Number of patients n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;500</td>
<td>00 (00)</td>
</tr>
<tr>
<td>500-200</td>
<td>23 (46)</td>
</tr>
<tr>
<td>199-50</td>
<td>16 (32)</td>
</tr>
<tr>
<td>&lt;50</td>
<td>11 (22)</td>
</tr>
<tr>
<td>Total</td>
<td>50 (100)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Respiratory symptoms</th>
<th>Number of patients n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>44 (88)</td>
</tr>
<tr>
<td>Cough</td>
<td></td>
</tr>
<tr>
<td>• Productive cough</td>
<td>24 (48)</td>
</tr>
<tr>
<td>• Dry cough</td>
<td>08 (16)</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>16 (32)</td>
</tr>
<tr>
<td>Hemoptysis</td>
<td>04 (08)</td>
</tr>
</tbody>
</table>

HIV: Human immunodeficiency virus
(PCP) 4 (8%), fungal infection seen in 1 (2%) of the cases (Table 4).

**DISCUSSION**

In the present study, total number of male patients is 41 (82%) and females are 9 (18%). Out of total 50 patients, 17 (34%) cases were in the age group of 15-29 years, 31 (62%) cases were in the age group of 30-49 years and 1 (2%) case was in the age group of more than 50 years. These findings were comparable to the data of global agricultural concept scheme and NACO, in which maximum number of patients were in the age group of 30-49 years. It shows the prevalence of HIV is more in reproductive life years.

In the present study, maximum patients 35 (70%) had heterosexual route of transmission. These findings were similar to the study conducted by Ramesh and Gandhi et al. in Karnataka, in 2015, in which they observed a heterosexual mode of transmission in 84.7% of the total cases.

In the present study, fever was the most common presenting symptom in 44 (88%) of the cases followed by cough which was present in 32 (64%) of the cases. Productive cough was present in 24 (48%) of the cases, whereas dry cough was present in 8 (16%) of the cases. Dyspnea was present in 16 (32%) of the cases; chest pain was present in 6 (12%) cases, and hemoptysis was present in 4 (8%) of the cases.

In the present study, the most common OI is pulmonary tuberculosis 33 (66%) followed by bacterial pneumonia 12 (24%) and others are PCP 4 (8%), fungal infection 1 (2%) which is comparable to the study done by Tanzania et al., in which tuberculosis was seen in 75% of the cases. Study done by Wallace et al., in USA maximum number of cases, was of PCP 45% and bacterial pneumonia 42%. In a study conducted by Kumarswamy et al., in 1995, in Tamil Nadu, they observed tuberculosis infection in maximum number of cases. In another study conducted by Sreevidya and Dias, in 2012, they observed that mycobacterium tuberculosis is the most common pathogen causing OIs in HIV-positive individuals.

This shows that, in developing countries, the commonest OI is tuberculosis while, in developed countries, it is PCP and bacterial pneumonia.

**CONCLUSION**

Tuberculosis is the most common disease in HIV-infected individuals, other than tuberculosis, other bacterial and fungal infections are also common when CD4 cell counts decreased to <200. Low CD4 count is a sign of decreased immunity and higher chances of OIs. HIV and tuberculosis co-infection is a major problem in India. Early diagnosis of HIV infection and initiation of antiretroviral therapy can be helpful in preventing the patients from OIs.

**REFERENCES**


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Serum Magnesium Levels in Type 2 Diabetes Mellitus

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Abstract

Introduction: Magnesium deficiency is proposed as a factor in the pathogenesis of diabetic complications. Hypomagnesemia can be both a cause and a consequence of diabetic complications.

Materials and Methods: This study was undertaken at MGM Hospital, Warangal, from August 2014 to October 2015. A total of 75 cases of Type 2 diabetes mellitus were taken for the study after satisfying the inclusion and exclusion criteria.

Results: The serum magnesium levels among cases and controls were 1.88 ± 0.28 mg/dl and 2.1 ± 0.29 mg/dl, respectively.

Conclusion: There was a significant reduction in serum magnesium levels in diabetics compared to the controls. There was a significant correlation between magnesium levels and level of control of diabetes. Uncontrolled diabetics had a low level of serum magnesium.

Key words: Deficiency, Magnesium, Type 2 diabetes mellitus

INTRODUCTION

Diabetes mellitus (DM) refers to a group of common metabolic disorders that share the phenotype of hyperglycemia. Several distinct types of DM are caused by a complex interaction of genetics and environmental factors. Depending on the etiology of the DM, factors contributing to hyperglycemia include reduced insulin secretion, decreased glucose utilization, and increased glucose production. The metabolic dysregulation associated with DM causes secondary pathophysiologic changes in multiple organ systems, leading to microvascular (retinopathy, nephropathy, and neuropathy) and macrovascular (coronary heart disease, peripheral arterial disease, and cerebrovascular disease).¹ Low magnesium status has repeatedly been demonstrated in patients with Type 2 diabetes. Magnesium deficiency appears to have a negative impact on glucose homeostasis and insulin sensitivity in patients with Type 2 diabetes.²

Magnesium deficiency has been found to be associated with microvascular disease in diabetes. Hypomagnesemia has been demonstrated in patients with diabetic retinopathy, lower levels of magnesium predicting a greater risk for diabetic retinopathy. Magnesium depletion has also been associated with arrhythmogenesis, vasospasm, platelet activity, and hypertension.³ 25-39% of outpatient diabetics has low concentrations of serum magnesium⁴ and numerous studies have shown lower serum magnesium concentrations in Type 2 diabetics compared to healthy controls.⁵,⁶ The reasons why magnesium deficiency occurs in diabetes are not clear but may include increased urinary loss, lower dietary intake, or impaired absorption of magnesium compared to healthy individuals.⁷

Several studies have reported increased urinary magnesium excretion in Type 1 and 2 diabetes,⁸,¹¹ some reporting a correlation between glycemic control and urinary magnesium loss.¹⁰

Magnesium is involved in insulin secretion, binding, and activity. Cellular deficiency of magnesium can alter...
the membrane-bound sodium-potassium-adenosine triphosphatase which is involved in maintaining the gradient of sodium and potassium and also in glucose transport.\textsuperscript{12}

Low dietary intake may also contribute to low magnesium status in diabetics. Patients with Type 2 diabetes are often overweight and may consume a diet higher in fat and lower in magnesium density than non-diabetics. However, the few studies that have reported magnesium intake in Type 2 diabetes are equivocal.\textsuperscript{6,13} Impaired intestinal absorption might also contribute to low magnesium status in diabetics. However, there are no published data on magnesium absorption in humans with diabetes. Despite the growing realization of the importance of magnesium in human health and disease, measurement of magnesium status remains problematic. Serum magnesium concentrations can be normal despite depletion of intracellular magnesium.\textsuperscript{14}

Magnesium deficiency may result in disorders of tyrosine-kinase activity on the insulin receptor, event related to the development of post-receptoral insulin resistance and decreased cellular glucose utilization that is, the lower the basal Mg, the greater the amount of insulin required to metabolize the same glucose load, indicating decreased insulin sensitivity. Experimental researches have shown that patients with diabetic retinopathy present low concentration of plasma magnesium, disposing to a higher risk of advanced retinopathy.

In Type 2 diabetic patients with microalbuminuria or clinical proteinuria, it showed a significant decrease in serum ionized Mg levels. It was also observed a significant negative correlation between serum ionized Mg and hemoglobin A1c (HbA1c) and triglycerides in both microalbuminuria and clinical proteinuria groups. In elderly Type 2 diabetics, Paolisso et al. demonstrated that oral supplementation of magnesium for 4 weeks resulted in lower fasting plasma glucose levels, increased plasma and erythrocyte magnesium levels and an increase in B-cell response to glucose.

The present study was undertaken with an aim to correlate serum magnesium levels with micro and macrovascular complications of diabetes - retinopathy, nephropathy, neuropathy and ischemic heart disease, and peripheral vascular disease.

**MATERIALS AND METHODS**

**Source of Data**

Patients with Type 2 diabetes admitted in the MGM Hospital between August 2014 and October 2015 were included in the study. Furthermore, 35 non-diabetic patients admitted during this period were also included in the study under the control group.

**Method of Collection of Data**

Around 75 patients with Type 2 DM and 35 controls admitted to the MGM Hospital underwent the following tests:

1. Fasting blood sugar (FBS)
2. Postprandial blood sugar (measured 2 h after a standard meal)
3. Fasting serum magnesium levels (Calmagite dye method), normal 1.8-2.5 mg/dl
4. 24 h urinary protein
5. Urine routine
6. Electrocardiography
7. Fundoscopy
8. Renal function test

Diabetics was divided into controlled (HbA1c <7) and uncontrolled (HbA1c >7).

**Inclusion Criteria**

All cases of Type 2 DM and age- and sex-matched non-diabetic patients admitted to the MGM Hospital.

**Exclusion Criteria**

1. Patients with chronic renal failure
2. Acute myocardial infarction in last 6 months
3. Patients on diuretics
4. Patients receiving magnesium supplements or magnesium-containing antacids
5. Malabsorption or chronic diarrhea
6. Patients with a history of alcohol abuse
7. Pregnant women with hypertension, proteinuria, and eclampsia
8. Patients with a history of epilepsy.

**RESULTS**

**Study Design**

A comparative study consisting of 75 diabetic patients and 35 controls was undertaken to investigate the change pattern of serum magnesium in DM cases when compared to controls and magnesium levels in relation to complications of DM.

The mean age of the diabetics was 59.56 ± 9.70 and 58.66 ± 10.26 in controls.

Sex distribution in diabetics was male 57.33\% and females 42.67\%, whereas in controls males 57.14\% and females 42.86\%. The maximum number of patients was in the age group of 51-60 years, i.e., 36.0\%.

The mean FBS levels among cases and controls were 206 mg/dl and 94.86 mg/dl, respectively. Among cases,
mean FBS was found to be high as compared to controls, probably because of poor diabetic control. The mean serum creatinine levels among cases and controls were 0.96 and 0.90 mg/dl, respectively.

The mean serum magnesium levels in cases and controls are 1.88 and 2.1 mg/dl with a \( P < 0.003 \), which is statistically significant. Although the exact reason in not known, this could probably be explained on the basis of increased urinary loss, low dietary intake, or impaired absorption of magnesium in diabetic patients.

Hypomagnesemia was seen in 38.6\% of the cases, whereas only 2.9\% of the controls had hypomagnesemia.

The mean serum magnesium levels among patients with uncontrolled diabetes were lower as compared to patients with controlled diabetes, which was statistically significant (\( P < 0.001 \)). Hyperglycemia directly causes suppression of magnesium.

Of the 75 diabetic patients, 33 (44\%) were on oral hypoglycemic agents (OHAs), 12 (16\%) were on insulin alone, and 30 (40\%) were on both OHAs and insulin. The mean serum magnesium levels in the OHA group, insulin group, and OHA+ insulin group were 1.99, 1.73, and 1.82 mg/dl, respectively. The serum magnesium levels were significantly lower in the insulin-treated group as compared to the OHA treated group (\( P < 0.013 \)).

This is because insulin causes shift of magnesium from extracellular to intracellular compartment causing low serum magnesium levels (Tables 1-7 and Figures 1-3).

**DISCUSSION**

The present study included 75 diabetic patients (cases) and 35 non-diabetic patients (controls). Serum magnesium levels were determined in all the subjects.

The present study had diabetic patients ranging from 41 to 80 years of age. The mean age in cases and controls was 59.56 and 58.66 years, respectively. Male patients in cases and controls were 57.33\% and 57.14\%, respectively, and females were 42.67\% and 42.86\%, respectively.

In this study, mean serum magnesium levels in cases and controls were 1.88 ± 0.28 mg/dl and 2.10 ± 0.29 mg/dl, respectively, which means diabetics are having low serum magnesium level compared to non-diabetics, with a \( P < 0.003 \) which is statistically significant.

<table>
<thead>
<tr>
<th>Table 1: Age distribution</th>
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<tbody>
<tr>
<td>Age in years</td>
</tr>
<tr>
<td>41-50</td>
</tr>
<tr>
<td>51-60</td>
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<tr>
<td>61-70</td>
</tr>
<tr>
<td>71-80</td>
</tr>
<tr>
<td>&gt;80</td>
</tr>
<tr>
<td>Total</td>
</tr>
<tr>
<td>Mean±SD</td>
</tr>
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| SD: Standard deviation |

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<thead>
<tr>
<th>Table 2: Sex distribution</th>
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<tbody>
<tr>
<td>Sex</td>
</tr>
<tr>
<td>Male</td>
</tr>
<tr>
<td>Female</td>
</tr>
<tr>
<td>Total</td>
</tr>
</tbody>
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<table>
<thead>
<tr>
<th>Table 3: Mean pattern of FBSs and serum creatinine levels</th>
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<tbody>
<tr>
<td>FBS/Serum creatinine</td>
</tr>
<tr>
<td>FBS (mg/dl)</td>
</tr>
<tr>
<td>Serum creatinine (mg/dl)</td>
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</tbody>
</table>

FBS: Fasting blood sugar

<table>
<thead>
<tr>
<th>Table 4: Serum magnesium levels in cases and controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum magnesium (n=1.8-2.5 mg/dl)</td>
</tr>
<tr>
<td>Range (Min-Max)</td>
</tr>
<tr>
<td>Mean±SD</td>
</tr>
<tr>
<td>95% CI</td>
</tr>
<tr>
<td>( P )</td>
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SD: Standard deviation, CI: Confidence interval

<table>
<thead>
<tr>
<th>Table 5: Comparison of serum magnesium levels between cases and controls</th>
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</thead>
<tbody>
<tr>
<td>Serum magnesium (mg/dl)</td>
</tr>
<tr>
<td>&lt;1.8</td>
</tr>
<tr>
<td>1.8-2.5</td>
</tr>
<tr>
<td>&gt;2.5</td>
</tr>
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<thead>
<tr>
<th>Table 6: Effect of level of control of DM on serum magnesium</th>
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<tbody>
<tr>
<td>Serum magnesium (n=37)</td>
</tr>
<tr>
<td>Range (Min-Max)</td>
</tr>
<tr>
<td>Mean±SD</td>
</tr>
<tr>
<td>95% CI</td>
</tr>
<tr>
<td>( P )</td>
</tr>
</tbody>
</table>

SD: Standard deviation, CI: Confidence interval, DM: Diabetes mellitus
Serum magnesium levels were low in Type 2 diabetics when compared to controls.

Levels of serum magnesium were further lower in uncontrolled Type 2 diabetics than those in whom diabetes was controlled.

3. Hypomagnesemia was associated with diabetic retinopathy and diabetic nephropathy.

4. No correlation was found in respect to neuropathy and ischemic heart disease.

5. More the duration of diabetes and the levels of FBS, lower was the serum magnesium levels.

6. Patients on insulin had lower levels of serum magnesium as compared to patients on OHAs.

7. Hypomagnesemia is a factor in Type 2 diabetes and associated with various complications. Hence, it is worth measuring serum magnesium levels in patients with type DM and probably correlates their relationship with various complications.

**REFERENCES**


**CONCLUSION**

1. Serum magnesium levels were low in Type 2 diabetics when compared to controls.

2. Levels of serum magnesium were further lower in uncontrolled Type 2 diabetics than those in whom diabetes was controlled.

3. Hypomagnesemia was associated with diabetic retinopathy and diabetic nephropathy.

4. No correlation was found in respect to neuropathy and ischemic heart disease.

5. More the duration of diabetes and the levels of FBS, lower was the serum magnesium levels.

6. Patients on insulin had lower levels of serum magnesium as compared to patients on OHAs.

7. Hypomagnesemia is a factor in Type 2 diabetes and associated with various complications. Hence, it is worth measuring serum magnesium levels in patients with type DM and probably correlates their relationship with various complications.
Evaluation of Perianal Fistulae using Magnetic Resonance Imaging

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INTRODUCTION

A perianal fistula is an inflammatory condition that affects the region around the anal canal with a presence of a fistulous tract across the anal sphincters, usually caused by an abscess. Perianal fistula has a high tendency to recur because of undetected infection at surgery, causing significant morbidity, and often requires repeated surgical treatments.1

In most of the cases, the track of the fistula has a relatively straight course between the external orifice and the internal opening in the anal canal (usually a posterior crypt). There is also a group of fistulas with a complex, branched, and high course, especially in patients after previous surgeries or patients with infections such as tuberculosis and Crohn’s disease.

Difficulties in the assessment of such tracts may lead to unsuccessful blind attempts at tract delineation during surgery. These attempts may be followed by formation of a false canal and orifice, and, in consequence, by
unnecessarily extensive surgery. Blind surgery favors the formation of pathological granulation tissue-inflammatory foci, while a too aggressive or too conservative operation causes disease recurrence or development of complications such as anal sphincter injury and a fecal incontinence.²

**Normal Magnetic Resonance Imaging (MRI) Anatomy of the Anal Sphincter**

The external anal sphincter (a striated muscle) is clearly visualized on MRI. It is hypo-intense on T1-weighted (T1W), T2-weighted (T2W), and fat-suppressed T2W images, and is bordered laterally by the fat in the ischioanal fossa. The internal sphincter (a smooth muscle) is hypo-intense on T1W and T2W TSE images and is relatively hyper intense on PD images (Figures 1a and b, 2a-c). The coronal images depict the levator ani muscle (Figure 2d), the identification of which is important to distinguish supraleaver from infraleaver infections.

**MATERIALS AND METHODS**

**Inclusion Criteria**

1. All patients (indoor and OPD) with clinical suspicion of perianal fistulae referred for MRI, irrespective of age and sex.
2. Patients operated previously on the pelvis and presenting with a perianal opening, with or without discharge.

**Exclusion Criteria**

- Patients with metallic implants (cardiac pacemakers, cochlear implants, tissue expanders, ocular prostheses, dental implants, neurostimulators, bone growth stimulators, implantable cardiac defibrillators, implantable drug infusion pumps, etc.)
- Claustrophobic patients.

MRI Machine PHILLIPS 1.5 Tesla (Achieva) was used for scanning the patients.

**Protocol**

- Patient positioning: Supine.
- Type of coil: Torso-axial coil.

**MRI Sequences**

- Axial T1 TSE
- Axial T2 TSE
- Axial T2 fat sat
- Coronal T2 TSE
- Coronal T2 fat sat
- Coronal PD SPAIR.

**RESULTS**

MRI scans were performed in 30 patients, with a clinical diagnosis of perianal fistula, out of which 4 patients had blind ending sinus tracts. Hence, the remaining 26 patients with a fistulous tract were considered in the study.

The most common age group involved in our study was the 51-60 years age group, with 9 patients out of 26 (35%) (Table 1).

In our study, all the patients with fistulas were males (100%) (Table 2). The most common type of fistula seen was the inter-sphincteric type of fistula, seen in 14 patients out of
26 (54%) (Table 3, Figure 3a and b). Associated ischiorectal abscess was seen in 7 out of 26 patients (27%), out of which 5 were trans-sphincteric fistulas out of 7 patients (71%) (Figure 4a and b). The remaining two ischiorectal abscess was associated with an intersphincteric fistula (Table 4).

Fistulous tracts crossing over to the opposite side were seen in 6 patients giving the appearance of horse-shoe fistulas, out of which 5 were trans-sphincteric type of fistulas (83%), and all the 6 horse-shoe fistulas were infrallevator, with none seen above the level of levatorani muscles (Table 4 and Figure 5).

About 3 patients were previously operated for fistulas, following which they had a recurrence on the same side, two of which were single fistulous tracts with branching (complex), and 1 single, linear, non-branching tract. Of the recurrent fistulas, 2 were inter-sphincteric type of fistulas and 1 was extra-sphincteric (Park’s classification).

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**Table 1: Age wise distribution of fistulas**

<table>
<thead>
<tr>
<th>Age group (in years)</th>
<th>Number of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>11-20</td>
<td>1</td>
</tr>
<tr>
<td>21-30</td>
<td>7</td>
</tr>
<tr>
<td>31-40</td>
<td>4</td>
</tr>
<tr>
<td>41-50</td>
<td>3</td>
</tr>
<tr>
<td>51-60</td>
<td>9</td>
</tr>
<tr>
<td>61-70</td>
<td>2</td>
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**Table 2: Sex wise distribution of cases**

<table>
<thead>
<tr>
<th>Gender</th>
<th>Number of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>26</td>
</tr>
<tr>
<td>Female</td>
<td>0</td>
</tr>
</tbody>
</table>

**Table 3: Type of fistulas (Park’s classification)**

<table>
<thead>
<tr>
<th>Type of fistula (Park’s classification)</th>
<th>Number of fistulas</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intersphincteric</td>
<td>14</td>
</tr>
<tr>
<td>Transsphincteric</td>
<td>13</td>
</tr>
<tr>
<td>Extrasphincteric</td>
<td>0</td>
</tr>
<tr>
<td>Suprasphincteric</td>
<td>0</td>
</tr>
</tbody>
</table>

**Table 4: Complex fistulas**

<table>
<thead>
<tr>
<th>A. Type of fistula</th>
<th>Deviation from linear fistulous tracts</th>
</tr>
</thead>
<tbody>
<tr>
<td>I. Horse-shoe fistula</td>
<td>Intersphincteric</td>
</tr>
<tr>
<td></td>
<td>Transsphincteric</td>
</tr>
<tr>
<td>II. Abscess formation</td>
<td>Intersphincteric</td>
</tr>
<tr>
<td></td>
<td>Transsphincteric</td>
</tr>
<tr>
<td>III. Branching/ramifications</td>
<td>Intersphincteric</td>
</tr>
<tr>
<td></td>
<td>Transsphincteric</td>
</tr>
</tbody>
</table>

Out of the 26 patients, 14 were complex fistulas (associated with abscess or branching tracts) (54%), 12 were simple fistulas (46%) (Figures 6a-d). About 1 patient had extrapulmonary tuberculosis and showed multiple perianal fistulas. Nearly 16 patients from our study population were alcoholics, 19 were chronic smokers, 16 people led a sedentary lifestyle with reduced physical activity, 9 were diabetics, 23 patients diet consisted of spicy food, and 17 patients had irregular bowel habits. To determine the association, we performed MRI fistulography in 23 controls, of which, 6 were alcoholics, 10 chronic smokers, 7 led a sedentary lifestyle, 14 were diabetics, 5 persons diet consisted of spicy food, and 7 had irregular bowel habits (Table 5).

All the patients were operated with the post-operative period being uneventful over a 6 month follow-up.

**DISCUSSION**

This is an observational study evaluating various types of perianal fistulas using MRI, studying the normal imaging anatomy of the perianal region, emphasizing the value of pre-operative MRI, and assessing the probable predisposing factors for perianal fistulas.

Perianal fistulas constitute a heterogenic group of pathologies of the terminal part of the gastrointestinal tract and perineal area, jointly termed as anorectal malformations. These are canals filled with granulation tissue and surrounded by thick fibrous tissue. Most of the fistulas are of glandular origin – cryptogenic – and a relatively straight tract starting in the perianal area, with the internal orifice in the anal canal, at the level of the crypt. The portals of infection may include anal fissure, post-operative wounds, anal injuries, and neoplasms of that area. More prone to complications are patients on immunosuppression, HIV-infected.

Initial diagnostics of perianal fistula is based on history-taking and physical examination which should include a detailed anal inspection with a rectal examination. This allows for a correct diagnosis in 48% of cases. Frequently, the internal orifice is narrowed, small, or periodically closed. If the internal orifice with an infected inter-sphincteric gland is not removed, and if all additional canals of the fistula are not found and properly drained or also removed, then the probability of recurrence is high.

Fistulography is the most traditional of the radiologic techniques. It is also the most unreliable and difficult to interpret as the sphincter complex is not visualized and the position of the levator sling has to be inferred. Moreover,
secondary fistulous tracts often fail to fill with contrast material. Furthermore, the level of the internal opening in the anal canal is difficult to visualize because of the absence of precise anatomic landmarks.

Anal endosonography, while promising much, has also proved inferior to expert clinical assessment. The sphincter mechanism and inter-sphincteric space are usually well visualized with endosonography, but the external sphincter can be difficult to visualize in some individuals. In addition, infection cannot be distinguished from fibrosis with this technique, and insufficient depth penetration can result in failure to identify secondary ramifications and more distant sepsis.

Computed tomography is performed with rectally and IV administered contrast media. The attenuation values for the sphincters, levator ani, fibrotic fistulous tracts, and active fistulas are so similar that it is difficult to characterize these structures accurately, unless the track contains gas or leaked contrast material.

The MRI appearance of this condition shows greater concordance with surgical findings than does any other imaging modality. MRI in the axial and coronal planes demonstrates fistulous tracks in relation to the sphincter complex, ischiorectal fossa, and levator plane. Imaging in the sagittal and oblique planes is helpful in selected cases (e.g., Anovaginal or presacral disease). 

Figure 2: (a) Axial T1-weighted image shows the normal hypointense internal anal sphincter (white arrow), and the ischiorectal fossa (red arrow). (b) Axial T2-weighted (T2W) image shows the normal hypointense external (orange arrow) and internal anal sphincters (White arrow). (c) Axial proton density image shows the hyperintense normal internal sphincter (yellow arrow). (d) Coronal T2W image shows the normal levator ani muscle (black arrow)

Figure 3: (a) Axial T2-weighted (T2W) showing an intersphincteric hyperintense tract between the two anal sphincters on left side (white arrow). (b) Coronal T2W showing an intersphincteric infralevator hyperintense tract on left side (yellow arrow)

Figure 4: (a and b) Axial T2-weighted and axial proton density images shows a hyperintense fluid collection in right ischiorectal fossa communicating with a trans-sphincteric hyperintense fistulous tract (yellow arrow)

Figure 5: Coronal T2-weighted image shows a hyperintense trans-sphincteric tract, with its external opening in left perianal region, extending in left perianal region and crossing midline in infralevator region to the right side (yellow arrow)
The anal canal extends from the levator ani muscle cranially to the anal verge caudally and is surrounded by the internal and external anal sphincters. The dentate line is an important landmark, as being the site of opening of the anal glands; it is considered the initial site of infection which initiates the fistula formation.

In our study, the most common type of fistula encountered according to Park’s classification was inter-sphincteric fistula, followed by trans-sphincteric fistula. These fistulas were classified into simple and complex types, depending on the presence of inter-sphincteric branching and associated ischiorectal abscess formation. Complex fistulas outnumbered simple ones in our study.

All three patients having undergone surgery for previous perianal fistula, developed recurrent fistulous tract on the same side. Sangwan et al. proved that the recurrence rate in patients after surgery due to a simple perianal fistula was about 6.5%.

Five patients had more than one fistulous tract (and external opening), with one of them being a confirmed case of extra-pulmonary tuberculosis.

MRI can detect fistulous extension with good localization in relation to surgically constant anatomical landmarks, especially in coronal sequences. The most important anatomical points for the surgeon were internal opening location which was described in clock orientation-external sphincter, course of the tract in relation to the sphincters and levator ani muscle. Pre-operative characterization of the anatomical course of the fistula and all associated infection is crucial and MRI helps to limit the recurrence and/or incontinence after surgery. This can be explained as it helps to avoid unnecessary wide exploratory dissection through the sphincter. While direct non imaging guided dissection may enforce the surgeon to do generous trans-sphincteric or supralevator dissection for detailed exploration, which is incriminated for postoperative incontinence. Moreover, the high possibility of missing other pathological contents, like the commonly reported side branches, horse-shoe extension, and abscesses, is the main causative etiology of postoperative recurrence.

Khera et al. performed contrast-enhanced studies for delineating abscess formation. In our study population, abscess formation was well delineated in 7 patients (without contrast study), on T2 SPAIR sequence, and was confirmed surgically.

Independent probable predisposing factors such as alcohol, smoking, diabetes, sedentary lifestyle, and irregular bowel habits had a significant association in the causation of perianal fistulas (Table 6).

### Table 5: Assessment of predisposing factors in cases and controls

<table>
<thead>
<tr>
<th>Predisposing factors</th>
<th>Cases</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alcoholism</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alcoholics</td>
<td>16</td>
<td>6</td>
</tr>
<tr>
<td>Non-alcoholics</td>
<td>10</td>
<td>17</td>
</tr>
<tr>
<td>Smoking</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Smokers</td>
<td>19</td>
<td>10</td>
</tr>
<tr>
<td>Non-smokers</td>
<td>7</td>
<td>13</td>
</tr>
<tr>
<td>Sedentary lifestyle</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sedentary lifestyle</td>
<td>16</td>
<td>7</td>
</tr>
<tr>
<td>Active lifestyle</td>
<td>10</td>
<td>16</td>
</tr>
<tr>
<td>Diabetes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetics</td>
<td>9</td>
<td>15</td>
</tr>
<tr>
<td>Non-diabetics</td>
<td>17</td>
<td>8</td>
</tr>
<tr>
<td>Diet</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Spicy food</td>
<td>23</td>
<td>20</td>
</tr>
<tr>
<td>Non-spicy food</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Irregular bowel habits</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Irregular bowel habits</td>
<td>17</td>
<td>7</td>
</tr>
<tr>
<td>Regular bowel habits</td>
<td>9</td>
<td>16</td>
</tr>
</tbody>
</table>

Cases: Patients having perianal fistulas. Controls: Patients not having perianal fistulas.

### Table 6: Association between predisposing factors and fistula formation

<table>
<thead>
<tr>
<th>Predisposing factor</th>
<th>Chi-square value</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alcohol</td>
<td>6.200</td>
<td>0.01</td>
</tr>
<tr>
<td>Smoking</td>
<td>4.426</td>
<td>0.03</td>
</tr>
<tr>
<td>Sedentary lifestyle</td>
<td>4.740</td>
<td>0.02</td>
</tr>
<tr>
<td>Diabetes</td>
<td>4.570</td>
<td>0.03</td>
</tr>
<tr>
<td>Diet</td>
<td>0.020</td>
<td>0.60</td>
</tr>
<tr>
<td>Irregular bowel habits</td>
<td>5.965</td>
<td>0.01</td>
</tr>
</tbody>
</table>
CONCLUSION

- Inter-sphincteric fistula with ramifications in its course is the most common type of perianal fistula.
- Complications are more often associated with a transsphincteric fistula.
- Extra-sphincteric and supra-sphincteric type of fistulas are very rare.
- MRI guides surgical management.
- Fat suppression T2 sequences were found to efficiently delineate perianal abscess formation, in a non-enhanced study.
- Patients dietary habits did not have a statistically significant association in the causation of perianal fistulas.

REFERENCES


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Role of Ultrasound Findings and Platelet Spleen Ratio in Assessing the Severity of Esophagogastric Varices in Patients with Cirrhosis of Liver

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Introduction

One of the main complications of cirrhosis of the liver is “portal hypertension.” The term portal hypertension was first coined by Gilbert and Villaret in 1906 when cirrhosis and high portal pressure were linked pathophysiologically.

Portal hypertension is defined by a pathologic increase in portal pressure, in which the pressure gradient between the portal vein and inferior vena cava (the portal pressure gradient [PPG]) is increased above the upper normal limit of 5 mm Hg. Portal hypertension becomes clinically significant when the PPG increases above the threshold value of 10 mm Hg (e.g., formation of varices) or 12 mm Hg (e.g., variceal bleeding, ascites). PPG values between 6 and 10 mm Hg represent subclinical portal hypertension.²,³

Portal hypertension causes esophagogastric varices. Bleeding from ruptured esophageal or gastric varices is the main complication of portal hypertension and a major cause of death.

As per existing guidelines in a case of portal hypertension, we are screening with upper gastrointestinal (GI) endoscopy to look for any esophagogastric varices present or not and grade the severity of varices. And then, we start the prophylactic measures like propanolol to prevent the first bleed. Doubts are expressed regarding the cost-effectiveness of universal screening with upper GI endoscopy.

“Empiric β blocker therapy for the primary prophylaxis of variceal hemorrhage is a cost-effective measure as the use of screening endoscopy to guide the therapy adds significant cost with only marginal increase in effectiveness.”

In this setting, if we can predict the severity of portal hypertension by a low cost- and non-invasive method, then we can use the upper GI endoscopy for only high-risk patients. Although the occurrence of esophageal varices and the time of GI bleeding in portal hypertension cannot be exactly predicted, there are some endoscopic, ultrasonographic (USG), and clinical signs associated with high risk of bleeding.

Some studies have shown good correlation between USG findings and severity of esophagogastric varices.

In this study, we make an attempt to predict the severity of varices based on USG findings and platelet count spleen diameter ratio its correlation with upper GI endoscopy.

**MATERIALS AND METHODS**

The study comprised 30 portal hypertensive patients who were submitted in Medical wards of Mahatma Gandhi Memorial Hospital, Warangal between February 2012 and July 2013.

A detailed clinical history was recorded regarding age, sex, duration of symptoms such as jaundice, distension of abdomen, hematemesis, and melena. All patients underwent complete clinical examination including detailed examination of GI system. Routine biochemical investigations and liver function tests were done in every patient.

Every recruited patient underwent USG and fiberoptic upper GI endoscopy. Platelet count spleen diameter ratio was calculated.

**Inclusion Criteria**

Cases of portal hypertension admitted in the Department of General Medicine and Gastroenterology in Mahatma Gandhi Memorial Hospital.

**Exclusion Criteria**

1. Cases of portal hypertension who are on β blockers
2. Cases of portal hypertension who underwent endoscopic sclerotherapy or endoscopic variceal ligation
3. Cases of portal hypertension who underwent transjugular intrahepatic portosystemic shunt or shunt surgery
4. Hepatocellular carcinoma
5. Primary hematological disorders
6. Active GI bleeding on admission
7. Previously known GI bleeding
8. Taking alcohol <6 months before enrollment
9. History of parenteral drug addiction
10. Other diseases with life expectancy of <1 year
11. Unstable medical condition.

**RESULTS**

The present study was carried out in the Department of Medicine, Mahatma Gandhi Memorial Hospital, Warangal, between February 2012 and July 2013. 30 portal hypertensive patients were recruited in this study. A detailed clinical history was recorded in each patient regarding age, sex, duration of symptoms, and history of alcohol intake.

All patients underwent complete clinical examination of GI system and other systems. Each patient was evaluated with routine biochemical parameters, liver function tests, and ascitic fluid analysis if present.

USG and fiberoptic GI endoscopy were done in every recruited patient. Platelet count spleen diameter ratio is calculated.

The result which was obtained as follows.

**Age Distribution**

All the cases were grouped according to their age into 3 as <20 years, 21-40 years, and 41-60 years (Table 1).

Of the 30 cases, 3 patients were below 20 years age, i.e., 10% of all cases. 15 patients were in the age group of 21-40 years, i.e., 50% of all cases. 12 patients, i.e., 40% were in the 41-60 years age group.

**Sex Distribution**

Of the 30 patients, 21 were males, i.e., 70% of all cases and 9 were females, i.e., 30% of all cases (Figure 1).

**Upper GI Endoscopy Findings**

In the patients of portal hypertension we studied, 18 patients had large grade varices, i.e., Grade III and Grade IV varices, 12 patients had small grade varices, i.e., Grade II varices (Table 2).

**Table 1: Age distribution**

<table>
<thead>
<tr>
<th>Age group</th>
<th>Number of cases (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;20 years</td>
<td>3 (10)</td>
</tr>
<tr>
<td>21-40 years</td>
<td>15 (50)</td>
</tr>
<tr>
<td>41-60 years</td>
<td>12 (40)</td>
</tr>
</tbody>
</table>
USG Characteristics

Out of 30 patients we studied, 24 patients had portal vein dilatation, i.e., 80% of all patients. The average portal vein diameter was 13.1 mm. 22 patients had splenic vein dilatation, i.e., 73% of all patients. The average splenic vein diameter was 12.4 mm.

Of the 30 patients, 22 patients had splenomegaly, i.e., 73% of all patients. The average spleen size was 15 cm. 20 out of 30 patients had shrunken liver, i.e., 66% of all patients. The average liver size was 13.6 cm.

24 out of 30 patients had altered, coarse echotexture of liver, i.e., 80% of all patients. Collaterals were present in 14 patients, i.e., 47% of all patients on USG.

USG characteristics of all patients are summarized in Table 3.

Comparison of USG characteristics in large varices and small varices patients (Table 4)

**Portal Vein Dilatation**
In large grade varices group, 18 patients had portal vein dilatation, i.e., 100% patients had portal vein dilatation. The mean portal vein diameter in this group was 14.5 mm.

In small grade varices group, 6 patients had portal vein dilatation, i.e. only 50% patients had portal vein dilatation. The mean portal vein diameter in this group was 10.9 mm (Figure 2).

**Splenic Vein Dilatation**
In large grade varices group, 16 patients had splenic vein dilatation, i.e., 88% of all patients had splenic vein dilatation. The mean splenic vein diameter was 14.1 mm. In small grade varices group, 4 patients had splenic vein dilatation, i.e., only 33% patients in this group had splenic vein dilatation. The mean splenic vein diameter was 9.75 mm.

**Splenomegaly**
In large grade varices group, 18 patients had splenomegaly, i.e., 100% patients had splenomegaly. The average spleen size in this group was 17.6 cm.

In small grade varices group, 4 patients had splenomegaly, i.e., only 33% patients had splenomegaly. The average spleen size in this group was 13.6 cm (Figure 3).

**Liver Echotexture**
In large grade varices group, 16 patients had altered or coarse echotexture of liver, i.e., 88% of all patients in the group had altered liver echotexture.
In small grade varices group, 8 patients had altered or coarse echotexture of liver, i.e. 67% of all patients in this group had altered liver echotexture (Figure 4).

Presence of Collaterals
About 12 of 18 patients in the large grade varices group had the presence of collaterals, i.e., 66% patients had collaterals. However, only 2 out of 12 patients in the small grade varices group had collaterals, i.e., only 17% patients had collaterals.

Platelet Count Spleen Diameter Ratio
In large grade varices group, the average platelet count spleen diameter ratio is 471 and the percentage of large grade varices group patients <858 is 100%.

In small grade varices group, the average platelet count spleen diameter ratio is 1438, and the percentage of small grade varices group patients >858 is 100%. The average platelet count spleen diameter ratio of all the 30 patients is 858 (Figure 5).

DISCUSSION
In the present study, 30 portal hypertensive patients were assessed with USG and fibreoptic upper GI endoscopy. Various USG parameters were compared with the severity of varices as detected by upper GI endoscopy.

In the present study, 100% patients had esophagogastric varices. In a similar study done by Sudhindra et al., 100% patients had esophageal varices.

In the present study, 60% patients had larger grade varices. Similar results were obtained in a study done by Sudhindra et al., in which 63% patients had larger grade varices.

In the present study, 80% patients had portal vein dilatation, with mean portal vein diameter as 13.1 mm. In a study done by Sudhindra et al., 83% patients had portal vein dilatation, with mean portal vein diameter as 15 mm.

In patients with larger grade varices, the average portal vein size is 14.5 mm as against 10.9 mm in patients with small grade varices. In a study done by Plestina et al., the average portal vein diameter in patients with larger grades varices was 15.38 ± 0.24 mm as against 12.43 ± 0.16 mm in patients with smaller grade varices.

In the present study, splenomegaly was found in 73% patients, and average spleen size was 15 cm. In a study done by Watanabe et al., splenomegaly was an indicator of the severity of varices.

In the present study, 66% patients with larger grade varices had collaterals, whereas only 17% of patients with small grade varices had collaterals. In a study done by Vilgrain...
et al., the best sign on USG to predict the severity of varices is the visualization of portosystemic shunts with a sensitivity of more than 80% and a specificity of 100%. Similar results were obtained in a study done by Subramanyam et al.7

In the present study, 80% patients had altered, heteroechoic liver echotexture. 88% of patients with larger grade varices had altered liver echotexture. Similar results were shown in a study done by Sudhindra et al.4 which concluded that altered, heteroechoic liver echotexture can be a sign of severe grades of varices.

In the present study, mean platelet count spleen diameter ratio is 838. In large grade varices group, mean platelet count spleen diameter ratio is 471 as against 1438 in small grade varices group. Similar results were obtained in a study group done by Testa et al.8

Thus, the present study has shown that there is a correlation between USG findings and platelet count spleen diameter ratio with the severity of esophagogastric varices.

CONCLUSION

USG of abdomen is a simple, convenient, and non-invasive method for assessing the severity of portal hypertensive patients and to predict the severity of esophagogastric varices indirectly.

Patients having portal vein diameter >14.5 mm, splenic vein diameter >14 mm, spleen size >17.6 cm, and the presence of collaterals on USG and platelet count spleen diameter ratio <858 were found to have higher grades of varices which were indirect evidence of the severity of portal hypertension. The above said parameters tend to predict the higher grades of varices when they occur in combination than they occur individually.

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Effect of Iron Deficiency Anemia on Glycation of Hemoglobin in Non-diabetics

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Abstract

Introduction: Glycosylated hemoglobin (HbA1c) is commonly used for monitoring glycemic control and as predictor of diabetes complications. Recently, HbA1c has also been recommended as a diagnostic test for diabetes mellitus by the American Diabetes Association.

Materials and Methods: About 63 non-diabetic, anemic patients, and 63 age-matched healthy subjects were enrolled in this study.

Results: The mean HbA1c (6.13% ± 0.6%) level in the patients with iron deficiency anemia (IDA) was higher than that in the control group (5.12% ± 0.5%) (P < 0.001).

Conclusion: It was found that IDA was common among the reproductive age group women. It was associated with shift in the HbA1c levels to higher side, primarily between 6.0% and 6.5%.

Key words: Diabetes mellitus, Glycosylated hemoglobin, Iron deficiency anemia

INTROCUCTION

Glycosylated hemoglobin (HbA1c) is on its way to celebrate the 50 years of existence and is being considered as one of the best achievements in the history of diabetes mellitus (DM).

HbA1c has been in use since 1980s as the “gold standard” for monitoring glycemic control and as a predictor of diabetic complications. Even though several conditions such as hemolytic anemia (lowers HbA1c) and aplastic anemia (raises HbA1c) tend to confound and interfere with HbA1c measurement, in most circumstances, HbA1c is a valid and reliable index of glycemic status. Recently, HbA1c has also been recommended as a diagnostic test for DM by the American Diabetes Association. HbA1c offers logistical advantages over the conventional oral glucose tolerance test as it requires a non-fasting random sample.

Iron deficiency is one of the most prevalent forms of malnutrition. Globally, 50% of anemia is attributed to iron deficiency. Ferritin is the storage form of iron, and it reflects the iron status accurately. An earlier study showed that reduced iron stores have a link with increased HbA1c, leading to false-high values of HbA1c in non-diabetic individuals. HbA1c is the most predominant fraction of HbA1, and it is formed by the glycation of terminal valine at the β-chain of Hb. It reflects the patient's glycemic status over previous 3 months.

Its alteration in other conditions such as hemolytic anemia, hemoglobinopathies, pregnancy, and vitamin B12 deficiency has been explained in a study conducted by Sinha et al. Although iron deficiency is the most common nutritional deficiency, reports of the clinical relevance of iron deficiency on HbA1c levels have been inconsistent.

HbA1c is widely used as an important marker of glycemic control, and it is of utter importance to exclude factors which could spuriously elevate its levels. Hence, we conducted a study in iron-deficient individuals with
MATERIALS AND METHODS

The present study was done over a period of about 1-year from July 2014 to August 2015 after approval by the Hospital Ethics Committee. Adult patients attending the outpatient clinics of Department of Medicine and patients admitted into medical wards of Kakatiya Medical College, MGM Hospital, Warangal, were screened for anemia as defined by WHO guidelines.

A total of 128 cases of anemia were detected of which 71 cases were diagnosed to have iron deficiency anemia. Among the 71 cases, the initial 63 consecutive patients satisfying the inclusion criteria were enrolled in the study.

Inclusion Criteria
- Presence of anemia as defined by WHO
  - Hb: <13.0 g/dl (adult males)
  - <12 g/dl (non-pregnant women)
- Microcytic, hypochromic picture in peripheral blood smear
- Serum ferritin: 
  - <9 ng/ml (in females)
  - <15 ng/ml (in males) suggestive of iron deficiency
- Normal fasting and postprandial plasma glucose levels
- Normal liver function tests
- Normal blood urea, serum creatinine levels.

Exclusion Criteria
The following patients were excluded from this study, those with:
- Glucose tolerance abnormalities (impaired glucose tolerance or DM)
- Hemoglobinopathies
- Hemolytic anemia
- Chronic alcohol ingestion
- Chronic renal failure
- Pregnant females
- History of blood transfusion in the past 3 months.

A detailed history was taken and physical examination was done.

The blood specimens were drawn after an overnight fast. Venous blood samples (3 ml) were drawn; 0.5 ml was taken into an EDTA-treated tube. A RIPL - 5000 fully automated analyzer and cell counter was used for the whole blood counts (Hb, hematocrit, mean corpuscular volume [MCV], and mean corpuscular Hb [MCH]); the serum ferritin levels were measured by using a Diater kit in automated analyzer, and the peripheral blood smears were examined in all the patients. The HbA1c levels were determined by turbidimetric immunoinhibition by using AIA 360 TOSOH AUTOMATED IMMUNOASSAY ANALYSER. Various biochemical tests were evaluated by standardized laboratory techniques.

This study was approved by the Ethics Committee of Kakatiya Medical College, Mahatma Gandhi Memorial Hospital, Warangal, Telangana State, India. An informed consent was obtained from all the subjects.

RESULTS

Estimation of complete hemogram including MCV, MCH, packed cell volume along with peripheral smear, serum ferritin levels, FBS, PLBS, HbA1c levels was done in all the 126 patients (63 cases and 63 controls) included in the study, during the study period.

All the patients enrolled in the study had normal FBS and PLBS levels, which confirmed their non-diabetic status.
- The Hb, serum ferritin levels (index of iron deficiency status) were low among the cases and the peripheral blood smear showed hypochromic microcytic picture in them.
- The Hb, serum ferritin and the HbA1c levels were normal in the control group ($P > 0.05$).
- The liver function tests, blood urea and serum creatinine levels were normal in all the patients.
- The serum HbA1c levels were significantly increased among the IDA patients as compared to those in the controls.

The mean HbA1c level in the patients with IDA (6.13% ± 0.57%) was higher than that in the control group (5.12% ± 0.30%) ($P < 0.001$).

Of the total of 126 patients enrolled in the study, case group consisted of 63 patients and the control group consisted of 63 patients. The youngest patient was 15 years and the oldest patient was 82 years old. The mean age of the study population was 38.41 ± 17.6 years and the mean of the control group was 39.17 ± 17.9 years. Those who were more than 40 years of age constituted 33% and the rest 67% were less than or up to 40 years of age. 21 patients, i.e., 33% with IDA were in the age group of 31-40 years and constituted the largest group (Table 1).

Out of 63 cases, 47 were females constituting about 75% of the study group and 16 were males constituting about
25%. Sex distribution was similar in the control group. Thus, iron deficiency anemia was more common among the females than the males (Table 2).

Out of 47 females with iron deficiency anemia, 13 females (28%) were in the age group of 31-40 years constituting the highest number, and out of 16 males with iron deficiency anemia, 8 males (50%) were in the age group of 31-40 years. In the study, iron deficiency anemia was more common in the age group of 31-40 years (Table 3).

Almost all patients were symptomatic with easy fatigability and tiredness. Easy fatigability was the most common symptom, present in all the 63 cases (100%). Dyspnea was the presenting complaint in 34 patients (54%), along with fatigability. Giddiness was presenting complaint in 11 patients constituting about 17%. Gastrointestinal blood loss was present in 10 cases (15%). Palpitations were present in 5 patients (8%) along with easy fatigability. Fever was the predominant complaint in 4 patients (6%) along with easy fatigability. Menorrhagia was present in 12 females (25% of females) (Table 4).

The most common clinical sign in the study group was pallor of tongue and conjunctiva which was present in all the 63 cases (100%) followed by ejection systolic murmur in the pulmonary area which was present in 32 cases (51%). Nail changes (koilonychia/platonychia) were present in 30 cases (48%) along with pallor. Koilonychia were present in 18 cases and platonychia in 12 cases. Along with pallor, bald tongue was present in 20 cases (32%), venous hum in 11 cases (17%), and pedal edema in 10 cases (16%) (Table 5).

The range of Hb was from 4.1 to 10.5 g/dl. The average Hb level among males with IDA was 7.59 g/dl and among females with IDA was 6.54 g/dl. The average Hb level among males in the control group was 14.03 g/dl and among females in the control group was 12.47 g/dl. The mean Hb in the case group was 6.84 ± 1.63 g/dl. The mean Hb in the control group was 12.87 ± 1.3 g/dl. These data provided evidence that Hb was indeed lower in anemic patients than in healthy controls, and the observed difference was statistically significant (P < 0.001) (Table 6).

In the study group, among 63 cases, 50 cases (79%) had severe anemia and 13 cases (21%) had moderate anemia. There were no mild anemia cases in the group. Out of 50 cases with severe anemia, 40 cases were females and 10 cases were males. Out of 13 cases with moderate anemia, 7 cases were females and 6 cases were males (Table 7).
Our results suggested that IDA was associated with higher concentrations of HbA1c. The earliest study to investigate the effects of iron deficiency anaemia on HbA1c levels was conducted by Brooks et al. who assessed HbA1c levels in 35 non diabetic patients having iron deficiency anaemia both before and after treatment with iron. They observed that HbA1c levels were significantly higher in iron deficiency anaemia patients and decreased after treatment with iron. The mechanisms leading to increased HbA1c levels were not clear. It was proposed that, in iron deficiency, the quaternary structure of the Hb molecule was altered, and that glycation of the globin chain occurred more readily in the relative absence of iron.\(^6\)

- Sluiter et al.\(^7\) tried to provide an explanation for the above findings. They proposed that the formation of HbA1c is an irreversible process and hence, the concentration of HbA1c in erythrocyte will increase linearly with the cell's age. For example, they found that in patients with normal blood glucose levels, but with very young red cells, as would be found after treatment of iron deficiency anaemia, HbA1c concentration was reduced. However, if iron deficiency has persisted for a long time, the red cell production rate would fall, leading not only to anaemia but also to a higher-than-normal average age of circulating erythrocytes and, therefore, increased HbA1c levels.\(^7\)

- Further studies by El-Agouza et al.\(^8,9\) and Cogan et al.\(^9\) showed that HbA1c levels were higher in patients with iron deficiency anaemia and decreased significantly upon treatment with iron. They argued that elevated HbA1c levels in iron deficiency anaemia could be explained by the assumption that if serum glucose remains constant, a decrease in the Hb concentration might lead to an increase in the glycated fraction.\(^8,9\) As evident from the above studies, the exact mechanism through which iron deficiency anaemia affects HbA1c levels still remains unclear. The explanations provided in the studies quoted above are merely speculation. Due to the variation in results obtained from these multiple studies, we were prompted to conduct our own study to investigate the effects of iron deficiency anaemia on HbA1c levels.

- Gram-Hansen et al.\(^10\) showed normal HbA1c concentrations in iron deficiency, which dropped to subnormal levels after iron supplementation.

- Rai and Pattabiraman\(^11\) investigated the different methods and no difference was detected among the colorimetric methods, ion-exchange chromatography, and affinity chromatography. The commonly performed immune turbidometric method was performed to determine the HbA1c levels in this study.

- Coban et al.\(^9\) found that among non-diabetic adults with iron-deficiency anemia, the A1c was 7.4% ± 0.3% before treatment and 6.2% ± 0.6% after treatment. Similar results were also found in studies carried out by Gram-Hansen et al.\(^10\) and Coban et al.\(^9\) Investigations performed on diabetic chronic kidney disease patients, and diabetic pregnant women showed increased A1c levels in iron deficiency anaemia, which was reduced following iron therapy.

- Likewise, Tarim et al.\(^12\) found that HbA1c in iron-deficient patients decreased from 7.6% ± 2.6% to 6.2% ± 1.4% after iron therapy (\(P < 0.05\)), despite similar glucose levels. We did not find such large shifts in HbA1c associated with iron deficiency, either because of the population-based nature of the sample or differences in HbA1c assays. In addition, we did not examine pregnant patients, and the previous studies of no pregnant patients may have included some adults with undiagnosed diabetes, as suggested by the HbA1c levels.

- Kim et al.\(^13\) investigated the influence of iron deficiency on HbA1c distribution among adults who were not known to have diabetes, over 7 years of the National Health and Nutrition Examination Survey. Of the 6666 female participants, 13.7% had iron deficiency and 30% of these had IDA. A much lower proportion of males (1.6%) had iron deficiency and 33% of these had IDA. When HbA1c values in women were adjusted for age and ethnicity, the difference between iron deficient and non-iron deficient became significant (5.33% vs. 5.27% [35 vs. 34 mmol/mol], \(P = 0.002\)). The authors found that iron deficiency in women of reproductive age was associated with a shift in HbA1c from<5.5% to 5.5-6.0% (<37 to 37-42 mmol/mol), although no association was found at higher levels, possibly owing to the lower number of participants in those groups. After adjusting for age and ethnicity, the authors concluded that HbA1c was higher in iron-deficient individuals and was likely to result in an upward shift of HbA1c distributions.
CONCLUSION

Our results showed that iron deficiency anemia was associated with higher proportions of HbA1c, which could cause problems in the diagnosis of uncontrolled DM in iron-deficient patients. This may have a practical application in diabetic individuals with IDA where HbA1c alone may give a false picture of poor glycemic control. The iron status must be considered during the interpretation of the HbA1c concentrations in DM. The iron replacement therapy is thus especially important in diabetic patients with iron deficiency, as it would also increase the reliability of the HbA1c determinations.

What does this mean on a wider scale?

Recent data has shown a surge in the incidence and prevalence of young onset obesity, many of whom are premenopausal females, at increased risk of iron deficiency. There has been a concomitant increase in HbA1c values in these participants considered at high risk of diabetes, owing to factors such as obesity. Data from England shows that the prevalence of pre-diabetes rose from 11.6% in 2003 to 35.3% in 2011 and in view of the rising prevalence of obesity; we would anticipate identifying a larger proportion of patients, with higher HbA1c values. If the estimated upward shift in HbA1c values seen with iron deficiency is combined with the apparent increased prevalence of pre-diabetes, it may result in a significant number of patients where the combination of the two will be sufficient to shift HbA1c values to move from a diagnosis of pre-diabetes to diabetes.

REFERENCES


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Effect of Hypertension on Lipid Profile of Individuals of Bihar State

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Abstract

Introduction: Hypertension and dyslipidemia are major risk factors for coronary artery disease (CAD) and account for >80% of death and disability in the low- and middle-income countries.

Materials and Methods: The study was conducted in the Department of Physiology, Patna Medical College and Hospital (PMCH), Patna. 60 patients of hypertension aged 40-50 years attending Outpatient Department of PMCH and 40 healthy volunteers were recruited in the present study to see the effect of hypertension on the lipid profile.

Results: Hypertensives showed a highly significant upper range of triglyceride (TG) with $P < 0.01$. Total cholesterol (TC) and very-low-density lipoprotein (VLDL) showed a partially significant upper range in hypertensives with $P < 0.1$, whereas high-density lipoprotein (HDL) and LDL showed no variations between these two groups with $P > 0.4$.

Conclusion: It was concluded that patients with hypertension are more likely to exhibit dyslipidemia, including elevated TC, TG, VLDL, and reduced HDL levels. So, they need a measurement of blood pressure and lipid profile at regular intervals to prevent the risk of CAD and stroke.

Key words: Blood pressure, Coronary artery disease, Low-density cholesterol, Triglyceride, Total cholesterol

INTRODUCTION

Hypertension and dyslipidemia are major risk factors for coronary artery disease (CAD) and account for >80% of death and disability in the low- and middle-income countries.¹,² The prevalence of hypertension is projected to increase globally, especially in the developing countries. The co-existence of the two risk factors has more than an additive adverse impact on the vascular endothelium, which results in enhanced atherosclerosis, leading CAD.³

In the recent years, rapid urbanization, increased life expectancy, unhealthy diet, and lifestyle changes have led to an increased rate of CAD. It is widely accepted that CAD is associated with hypertension and increased blood levels of triglyceride (TG), total cholesterol (TC), and low-density lipoprotein (LDL).⁴

The Framingham Heart Study data on the hypertensive population reported that more than 80% had at least on additional cardiovascular disease (CVD) risk factors such as obesity, glucose intolerance, and dyslipidemia.⁵ The risk of concomitant hypertension and dyslipidemia is more multiplicative than the sum of the individual risk factors.⁶

Dyslipidemia, one of the strong predictors of CVD, causes endothelial damage and loss of physiological vasomotor activity. The damage may manifest as elevated systemic blood pressure (BP).⁷

Hypertension, damages the endothelium through altered shear stress and oxidative stress, resulting in increased endothelial cell synthesis of collagen and fibronectin, reduced nitric oxide-dependent vascular relaxation, and increased permeability to lipoprotein. It is also associated with an upregulation of lipid oxidation enzymes, especially oxidized LDL contributing to atherosclerosis.⁸,⁹

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MATERIALS AND METHODS

Blood samples were obtained after an overnight fast. About 5 ml of blood was collected from the left antecubital vein. Of which, about 2 ml is transferred into an overfast vial and mixed well and centrifuged at a speed of 3000 revolutions per minute for 10 min to separate the plasma, which was used for biochemical analysis. Rest 3 ml of blood is transferred to the test tube, and this blood was allowed to clot to get serum. This serum was separated in a centrifuge tube at 3000 revolutions per min to get a clear sample of serum. This clear supernatant serum was used for biochemical investigation.

Estimation of Serum TC
Method: Enzymatic - (colorimetric trinder end point).

The reagents were allowed to attain room temperature before use.

<table>
<thead>
<tr>
<th>Blank</th>
<th>Standard</th>
<th>Sample</th>
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</thead>
<tbody>
<tr>
<td>Reagent R</td>
<td>1000 µl</td>
<td>1000 µl</td>
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<tr>
<td>Standard</td>
<td>-</td>
<td>10 µl</td>
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<tr>
<td>Sample</td>
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</table>

They were incubated for 5 min at 37°C and reading was done against the blank at 500 nm and calculation was made. The concentration of cholesterol in the sample is directly proportional to the intensity of red complex (red quinone), which was measured at 500 nm.

Calculation:

Cholesterol = Absorbance of sample/absorbance of standard × concentration of standard.

Estimation of Serum TG Method
Enzymatic: Colorimetric method contents were mixed and incubated for 5 min at 37°C. The reading was done against blank at 546 nm.

<table>
<thead>
<tr>
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<tr>
<td>Reagent R</td>
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<td>Sample</td>
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</tbody>
</table>

Calculation:

Serum TG = Absorbance of sample/absorbance of standard × n

n = Standard concentration.

Reference values: >150 mg/dl.

Estimation of High-density Lipoprotein (HDL)-cholesterol
Method: Phosphotungstate method.

Principle: Chylomicrons, LDL, and very-LDL (VLDL) are precipitated by addition of phosphotungstic acid and magnesium chloride. After centrifugation, the HDL fraction remains in the supernatant is determined with cholesterol oxidase/peroxidase amino phenol method.

Reference value: >40 mg/dl.

Calculation of LDL and VLDL by Friedewald’s formula:

LDL = TC − (HDL + VLDL)

VLDL = TG/5

Reference value:

LDL = Up to 190 mg/dl.

VLDL = 14-31.8 mg/dl.

BP
It was measured using standard BP measurement protocol after the patient had rested for 10 min. Two measurements were taken by a mercury sphygmomanometer, with at least a 5-min interval between successive measurements. Hypertension was defined as an average systolic BP ≥140 mm of Hg and diastolic BP ≥90 mm of Hg without antihypertensive medication.

RESULTS

Hypertensives showed a highly significant upper range of TG. Levels of TC and VLDL were also in partially significant higher range in hypertensive while HDL and LDL were of the same range in both groups (Table 1 and Figure 1).

<table>
<thead>
<tr>
<th>Lipid</th>
<th>Hypertensive</th>
<th>Normotensive</th>
<th>t</th>
<th>P</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>TC</td>
<td>193.93±20.46</td>
<td>180.17±17.08</td>
<td>1.83</td>
<td>&lt;0.1</td>
<td>PS</td>
</tr>
<tr>
<td>TG</td>
<td>164.02±17.87</td>
<td>144.09±15.33</td>
<td>2.44</td>
<td>&lt;0.05</td>
<td>HS</td>
</tr>
<tr>
<td>HDL</td>
<td>40.27±5.03</td>
<td>44.77±7.81</td>
<td>0.79</td>
<td>&gt;0.4</td>
<td>NS</td>
</tr>
<tr>
<td>LDL</td>
<td>112.28±19.78</td>
<td>106.21±18.81</td>
<td>0.80</td>
<td>&gt;0.4</td>
<td>NS</td>
</tr>
<tr>
<td>VLDL</td>
<td>32.80±4.57</td>
<td>28.80±3.07</td>
<td>1.42</td>
<td>&lt;0.1</td>
<td>PS</td>
</tr>
</tbody>
</table>

TG: Triglyceride, TC: Total cholesterol, VLDL: Very-low-density lipoprotein, HDL: High-density lipoprotein.
DISCUSSION

In this study, we investigated the relationship between serum lipid profile and hypertension among the individuals of Bihar state. Results of this study revealed that the mean value of serum TG was significantly higher and statistically significant. Levels of TC and VLDL were also in partially significant upper range in hypertensive than normotensive population. Various workers such as MacMohan et al., Coffin et al. (1990), and Samuelsson et al. had established a significant correlation between baseline BP and subsequent development of CAD. The management of these disorders, particularly in high-risk patients, requires multiple interventions, including dietary and pharmacological. There is a need to increase the awareness, both in the medical and patient communities, for early detection and treatment of these two conditions to decrease the incidence of future CAD.

REFERENCES

Clinical Study of Renal Profile of Acute Coronary Syndrome

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**Abstract**

**Background:** Markers of renal function have been incorporated in risk stratification of acute coronary syndrome (ACS). Global registry for acute coronary events risk score, Michigan percutaneous coronary intervention (PCI) risk score, Mayo PCI risk scores, etc. incorporate serum creatinine levels or creatinine clearance as one of the biomarkers in risk stratification with serum uric acid, limited data is available regarding its prognostic value in ACS.

**Objective:** To study the renal function parameters in patients of ACS.

**Methods:** A total of 100 patients who were admitted and fulfilled the inclusion/exclusion criteria were evaluated by history. Physical examination, electrocardiogram, echocardiography and renal function tests were performed.

**Result:** A total of 100 patients of diagnosed ACS were included in the study of which 75% were males and 25% were females. In 75 males, maximum 28 (37.3%) were in age group of 51-60 years followed by 16 (21.3%) in age group of 41-50 years and in 25 females maximum 11 (44.0%) were in age group 61-70 suggesting that ACS commonly occur in middle age group adults. Out of 100 diagnosed ACS patients, maximum (72%) were ST-segment elevation myocardial infarctions (STEMI) followed by 23% UA and 5% Non STEMI. Mean (+ standard deviation) serum creatinine value in STEMI patients was 2.20 + 1.61, was recorded indication mild to moderate renal insufficiency in ACS patients.

**Conclusion:** The long term morbidity and mortality is higher in those ACS patients who have deranged renal function, incorporating renal function parameters for regular assessment of patients at risk of developing ACS and measuring the renal function parameters in patient who have developed ACS at their first clinical visit in emergency department becomes important for risk stratification. Thus, it is concluded that renal function monitoring must be done in patients at risk or who have developed ACS for reducing the long term morbidity and mortality in such patients.

**Key words:** Acute coronary syndrome, Chronic kidney disease, Clinical profile, Creatinine, Creatinine clearance

**INTRODUCTION**

Cardiovascular diseases (CVDs) are currently are among the leading cause of death in industrialized as well as in emerging countries. Among CVDs coronary artery disease (CAD) is the most prevalent manifestation and is associated with high mortality and morbidity.¹ World Health Organization (WHO) estimates that CVDs are the number one cause of death globally with 9.4 million deaths each year of which 45% of deaths being due to coronary heart disease (CHD).² WHO estimates that more than 60% of the global burden of CHD occurs in developing countries. Globally, burden of CHD is projected to rise from around 47 million (in 1990) Disability-adjusted life years (DALYs) to 82 million DALYs in 2020. With India, DALYs lost per 1000 population were reported to be 20.³ Acute coronary syndrome (ACS) involves a range of thrombotic CADs. These are unstable angina (UA), ST-segment elevation myocardial infarctions (STEMI), and non-STEMI (NSTEMI).⁴ The clinical presentations of CAD include silent ischemia, stable angina pectoris, UA, myocardial infarction (MI), heart failure and sudden death.¹
Despite modern treatment, the rates of death, MI, and readmission of patients with ACS remain high.\(^1\)

A assessing the patient for cardiovascular risk is cornerstone in diagnosis and management of ACS. Risk stratification helps in appropriate referral of patients to and emergency department and assessment of the risk of future at the time of the initial assessment in the emergency department.\(^4,5\)

Different score based on different markers have been developed for risk stratification. Different risk scores that are validated include Thrombolysis in MI (TIMI) score, global registry for acute coronary events (GRACE) risk score, FRISC score, PURSUIT score.\(^6\) Among these, GRACE and TIMI risk scores are being used commonly used in clinical practice.\(^7\)

Different markers that are used in risk stratification include that of myocardial necrosis, inflammation, hemodynamic stress and neurohormonal activation, renal impairment, vascular injury, and accelerated atherosclerosis.\(^8\)

In addition to these, some novel biomarker and risk scores have been assessed for their prognostic value in risk stratification of ACS. These include high-sensitivity troponin (hs–cTn), CD40 ligand and interleukin-6, glycogen phosphorylase isoenzyme-BB (GP-BB), percutaneous coronary intervention (PCI) risk scores, angiographic risk scores.\(^7,8\)

Chronic kidney disease (CKD) is quite common with a prevalence of about 12% of adults.\(^9\) When CKD is considered, an independent association between renal dysfunction and mortality after ACS is reported.\(^10\) it has been reported that baseline renal dysfunction is a potent and easily identifiable determinant of outcome after an ACS.\(^11\) Therapeutic complexities are more in the management of patients with CKD presenting with ACS as compared to the general population because of the lack of well-designed randomized trials assessing therapeutic strategies in such patients.\(^12\)

Markers of renal function have been incorporated in risk stratification of ACS. GRACE risk score, Michigan PCI risk score, Mayo PCI risk scores, etc., incorporate serum creatinine levels or creatinine clearance (CrCl) as one of the biomarkers in risk stratification.\(^7\) with serum uric acid, limited data is available regarding its prognostic value in ACS.\(^13\)

Since limited data is available with renal profile of ACS patients in Indian scenario, we planned this research to study the renal parameters in ACS patients.\(^14-23\)

**Aims and Objectives**

To study the renal function parameters in patients of ACS in cardiac intensive care unit (ICU) of a tertiary care hospital.

**MATERIALS AND METHODS**

This open label, prospective, single center, observational, cross-sectional study was conducted in patients admitted at cardiac ICU of a tertiary care hospital. Institutional ethics committee (IEC) approved the study protocol. Study patients were screened at cardiac ICU for the recruitment criteria and those who fulfilled the inclusion and exclusion criteria were enrolled in study. Patients were given patient information sheet to understand the study details. Any questions concerning the study were answered. Then the informed consent was sought from each patient in an IEC approved informed consent form (ICF). The patients were recruited with following inclusion and exclusion criteria.

**Inclusion Criteria**

- Age >18 years
- Either gender
- Investigated and diagnosed cases of ACS in cardiac ICU.

**Exclusion Criteria**

- Not willing to participate in study or give informed consent.

Patients fulfilling these criteria were enrolled and ICF was signed. Study related parameters were then noted in case record forms (CRF). ICU case record papers were observed to record the data. The data collected includes demographic parameters such as registration number, age, sex, height, weight, and body mass index (BMI). The vital signs were recorded. The clinical history of the patient was also recorded from the case files and by direct questioning to the patient and it includes smoking history, any major illness such as diabetes, hypertension, or CKD. The findings of electrocardiogram (ECG) were noted.

As per the protocol in the management of ACS at this cardiac (ICU, all the blood investigations including biomarkers and renal function tests are routinely performed. From these investigation reports, blood sugar levels, troponin T result, serum creatinine, blood urea nitrogen (BUN), serum uric acid levels, serum albumin levels, urine routine and microscopy examination results, etc., were recorded in CRF. No active investigations on any patient were performed during the study. The CrCl was calculated for each patient with the help of following formula.

\[
\text{Creatinine clearance} = \left(\frac{140 - \text{Age}}{72}\right) \times \frac{\text{Body weight} \ (\text{kg})}{\text{Serum creatinine}}
\]

(To be multiplied by 0.85 if the patient is female).
Statistical Analysis
The collected data was analyzed using the SPSS software version 15. The data are presented as frequency and percentages. The mean and standard deviation (SD) were calculated. For quantitative data, student’s t-test were used and for qualitative data analysis, Chi-square test with or without Yates' correction were used. P < 0.05 was considered significant.

Chart 1 shows that in total, 75% patients were males and 25% patients were females.

RESULTS

Table 1 shows the age group wise distribution of males and females enrolled in the study. Out of total 75 males, 11 (14.7%) were 40 years or less, 16 (21.3%) were in between 41 and 50 years, 28 (37.3%) were in between 51 and 60 years, 12 (16.0%) were in 61-70 years age group, whereas 8 (10.7%) were 71 years or above. Out of total 25 females, the frequencies for females in given age group were 1 (4.0%), 1 (4.0%), 2 (8.0%) 11 (44.0%), and 10 (40.0%), respectively.

Chart 2 describes the smoking history of patients. No females had smoked anytime in their life. Out of 75 males, 40 (53.3%) had active smoking in their life.

Table 2 gives the gender wise distribution of mean age and BMI. The mean age of males was 54.5 + 12.7 and of females was 67.2 + 10.4. BMI in males was 25.1 + 2.1 and in females, it was 25.6 + 3.2.

Table 3 gives the diagnosis of the patients enrolled in to the study. Among ACS diagnosed in total 100 patients, maximum (72%) were STEMI followed by UA with 23% patients and NSTEMI with 5% of patients.

Table 4 shows that 67 (93%) patients with STEMI and 5 (100%) patients with NSTEMI had TnT positive. Only 5 (7.0%) patients with STEMI had negative result of TnT test.

Chart 3 describes percentage of ACS patients having serum creatinine levels within and above normal limits. Of 100

<p>| Table 1: Age group wise distribution of males and females in the study |</p>
<table>
<thead>
<tr>
<th>Age group</th>
<th>Gender (%)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Male</td>
<td>Female</td>
</tr>
<tr>
<td>&lt;40</td>
<td>11 (14.7%)</td>
<td>1 (4.0%)</td>
</tr>
<tr>
<td>41-50</td>
<td>16 (21.3%)</td>
<td>1 (4.0%)</td>
</tr>
<tr>
<td>51-60</td>
<td>28 (37.3%)</td>
<td>2 (8.0%)</td>
</tr>
<tr>
<td>61-70</td>
<td>12 (16.0%)</td>
<td>11 (44.0%)</td>
</tr>
<tr>
<td>≥70</td>
<td>8 (10.7%)</td>
<td>10 (40.0%)</td>
</tr>
<tr>
<td>Total</td>
<td>75</td>
<td>25</td>
</tr>
</tbody>
</table>

<p>| Table 2: Mean age and BMI of patients in the study |</p>
<table>
<thead>
<tr>
<th>Parameter</th>
<th>Gender</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Male</td>
<td>Female</td>
</tr>
<tr>
<td>Age (years)</td>
<td>54.5+12.7</td>
<td>67.2+10.4</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>25.1+2.1</td>
<td>25.6+3.2</td>
</tr>
</tbody>
</table>

Data presented as mean±SD, **P<0.05 considered significant, SD: Standard deviation, BMI: Body mass index, SD: Standard deviation

<p>| Table 3: Diagnosis of patients enrolled in the study |</p>
<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Number of patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>NSTEMI</td>
<td>5 (5.0)</td>
</tr>
<tr>
<td>STEMI</td>
<td>72 (72.0)</td>
</tr>
<tr>
<td>UA</td>
<td>23 (23.0)</td>
</tr>
<tr>
<td>Total</td>
<td>100 (100)</td>
</tr>
</tbody>
</table>

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

<p>| Table 4: TnT positivity among the patients diagnosed with STEMI or Non-STEMI in the study |</p>
<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Troponin-T, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive</td>
<td>Negative</td>
</tr>
<tr>
<td>STEMI</td>
<td>67 (93.0)</td>
</tr>
<tr>
<td>NSTEMI</td>
<td>5 (100)</td>
</tr>
</tbody>
</table>

STEMI: ST-segment elevation myocardial infarction, NSTEMI: Non ST-segment elevation myocardial infarction, TnT: Troponin-T
ACS patients in the study, 67% had serum creatinine within normal limits of 1.5 mg/dl where as 33% patients had value above 1.5 mg/dl suggesting deranged renal function in these patients.

Chart 4 describes the serum urea levels in ACS patients. Out of 100 patients, 66% had serum urea level above 40 mg/dl. About 34% patients had level in normal limits.

Table 5 describes the presence of hypertension, ischemic heart disease, and CKD in patients enrolled in study. About 61.1% STEMI, 40.0% NSTEMI, and 56.5% UA patients had hypertension; 19.4% STEMI, 40.0% NSTEMI, and 34.7% UA patients had IHD and 23.6% STEMI and 21.7% UA patients had CKD. No patients with NSTEMI had associated CKD illness.

Chart 5 describes the overall serum uric acid levels in ACS patients of which 90% had levels <7 mg/dl and 10% had values above normal that is more than 7 mg/dl.

Table 6 gives some of the major renal function parameters in patients of ACS. Mean values of serum creatinine in STEMI, NSTEMI, and UA were 2.20 + 1.91, 1.16 + 0.31, and 1.93 + 1.57, respectively. The mean value for CrCl in STEMI was 99.88 + 35.80, in NSTEMI was 117.20 + 5.19, and in UA was 100.89 + 32.36. The value of serum urea in STEMI, NSTEMI and UA were 72.67 + 59.19, 39.80 + 11.05, and 65.76 + 56.97. Mean serum uric acid concentration was 4.92 + 1.34, 4.20 + 1.32 and 4.48 + 1.37 foe STEMI, NSTEMI, and UA patients, respectively.

Table 7 describes urinary protein levels in ACS patients in the study. Of the 7 STEMI patients, 22.2% had nil proteins in urine, 38.9% had 1+ trace proteins, 18.1% had 1+, 13.9% had 2+, and 6.9% had 3+ grade protein excretions. No NSTEMI had grade 2+ or 3+ protein excretion, out of 23 UA patients, 47.8% had nil excretion, 17.4% had trace, and 1+, 8.7% had 2+ and 3+ proteins excretion in urine.

Table 8 shows the urinary albumin: Creatinine ratio (ACR) in ACS patients in the study. None of patients with NSTEMI had ACR >30. Of total 72.76.3% STEMI
patients and of total 23, 78.3% UA patients had ACR <30. Among STEMI patients, 11.1% had ACR between 500 and 1000, 5.5% had ACR in between 1001 and 1500 and 4.1% had ACR above 1500. Among UA patients, 13.1% had ACR between 500 and 1000 and only one patient had ACR in-between 1001 and 1500 and above 1500.

Table 9 shows serum homocystiene concentration in STEMI and UA groups. In only 12 patients (10 STEMI and 2 UA), serum homocystiene was determined as per the clinical need by the cardiologist. In 10 STEMI patients, mean values for serum homocystiene were 31.28 ± 7.18 and that for two UA patients were 37.66 ± 7.85.

DISCUSSION

In the field of cardiology, large-scale clinical trials have provided enormous data on the treatment and outcomes for hundreds of thousands of patients. Many of these efforts have focused on patients with ACS, which range STEMI to NSTEMI to UA. ACS represents a life-threatening manifestation of atherosclerosis. It is usually precipitated by acute thrombosis induced by a ruptured or eroded atherosclerotic coronary plaque, with or without concomitant vasoconstriction, causing a sudden and critical reduction in blood flow. WHO estimates that CVDs are the number one cause of death globally with 9.4 million deaths each year of which 45% of deaths being due to CHD.

STEMI is a clinical syndrome defined by characteristic symptoms of myocardial ischemia in association with persistent ECG ST elevation and subsequent release of biomarkers of myocardial necrosis. UA and NSTEMI are considered to be closely related conditions whose pathogenesis and clinical presentations are similar but of differing severity. Once it has been established that no biochemical marker of myocardial necrosis (troponin I [TnI], TnT, or the MB isoenzyme of creatine phosphokinase [CK-MB]) has been released, the patient with an ACS may be considered to have experienced UA, whereas the diagnosis of NSTEMI is established if a marker of myocardial injury has been released. of the number of available markers and assays that detect myocardial necrosis, the cardiac TnT and TnI and the creatinine kinase-MB (CK-MB) isoform are the most commonly used, with Tn gaining acceptance as the markers of choice in ACS.

CKD is defined as persistent kidney damage, as reflected by a glomerular filtration rate (GFR) of <60.0 ml per min per 1.73 m² of body surface area for more than three mortality in the follow-up of patients who have undergone coronary artery bypass grafting or a PCI and those who have suffered an acute MI. Also mild renal impairment is associated with an increased risk of CAD and stroke. Suggesting that CVD may develop early in the course of renal dysfunction.

With evolving new treatments for the management of ACS, risk stratification has become the centerpiece of initial evaluation for these patients. Risk stratification has now evolved more to include the assessment of the risk of future cardiac events, which can be predicated on the basis of clinical features and biomarkers at the time of the initial assessment in the emergency department. For evaluating risk of ACS, various risk scores have been developed and are used clinically. The TIMI and GRACE risk scores are recommended for risk stratification. GRACE score predict cumulative 6-month risk of mortality or MI, with predictor variables including age, heart rate, systolic blood pressure (SBP), creatinine level, Killip class of heart failure, cardiac arrest at admission, ST-segment deviation, and cardiac enzymes. Creatinine has been included in
many clinical scores to assess the prognosis of critically ill patients. In a study measuring CrCl on admission in patients with cardiogenic shock consecutive to ST elevation MI and for whom a PCI was performed, and independent strong association between CrCl on admission and 1-year-mortality was reported, which was significantly higher when CrCl was <67.5 ml/min.

With serum uric acid, hyperuricemia has been implicated as a marker of poor outcome, both in the general population and in patients with stroke and heart failure. There is limited data in the context of ACS with contradictory results. Given the role of renal function parameters association with ACS morbidity and mortality, we studied the renal function profile in diagnosed ACS patients at tertiary care hospital.

A total of 100 patients of diagnosed ACS were included in the study of which 75% were males and 25% were females. In 75 males, maximum 28 (37.3%) were in age group of 51-60 years followed by 16 (21.3%) in age group of 41-50 years and in 25 females maximum 11 (44.0%) were in age group 61-70 suggesting that ACS commonly occur in middle age group adults. This is consistent with age group range of 51-71 years in a study by Akerblom et al. Mean age in males was 54.5 years and in females was 67.2 years, which was statistically non-significant (P = 0.226). Smoking was common in males only with 53.3% males reported active cigarette smoking. No female had smoked ever in their life. The mean BMI varied in two genders and difference was statistically significant (P = 0.016). BMI is also an important risk factor for the development of ACS. In a study by Wolk et al.; the mean values of BMI in stable and unstable CAD were 28.8 + 4.7 and 30.5 + 5.7, respectively, and reported a positive relation between BMI and the risk of acute coronary events for even mildly elevated BMI values.

Out of 100 diagnosed ACS patients, maximum (72%) were STEMI followed by 23% UA and 5% NSTEMI. Tn are among the priority biomarkers in ACS and are used clinically to differentiate the establishment of ischemia in NSTEMI and UA. Out of 72 diagnosed STEMI patients, 67 (93%) had TnT test positive and 5 (7%) had negative results with TnT test. In STEMI patients with negative TnT-test, ECG remains the main tool for the diagnosis in combination with other biomarkers. With positive TnT and no ST-elevation in ECG, diagnosis of NSTEMI is established. Among the associated illnesses in ACS patients, CKD was present in 17 (23.6%) to total 72 STEMI patients and in 5 (21.7) of 23 UA patients.

CKD and ACS are highly prevalent and highly relevant clinically for patients, physicians, and healthcare systems. The short-term as well as long-term prognosis of ACS patients with poor renal function is worse than those with normal renal function. The risk of cardiovascular (CV) events and mortality is inversely proportional to the estimated GFR (eGFR). The independent association between renal dysfunction and mortality after ACS has been reported. Death from cardiac causes is 10-20 times more common in CKD patients than in age-and gender-matched population. In this study, renal function parameters such as serum creatinine, CrCl, serum urea, serum uric acid, and urinary ACR were estimated in diagnosed ACS patients during the course of hospital stay.

Mean (+SD) serum creatinine value in STEMI patients was 2.20 + 1.61, was recorded indication mild to moderate renal insufficiency in ACS patients. Shlipak et al. studied association of renal insufficiency with treatment and outcomes after MI in 130,099 elderly patients. Patients were categorized according to the initial serum creatinine level no renal insufficiency (creatinine level <1.5 mg/dl), Mild renal insufficiency (creatinine level, 1.5-2.4 mg/dl), or moderate renal insufficiency (creatinine level, 2.5-3.9 mg/dl), mild (hazard ratio, 1.68 [95% CI: 1.63-1.73]) and moderate (hazard ratio, 2.35 [CI: 2.26-2.45]) renal insufficiency were associated with substantially elevated risk for death during the first month of follow-up. 1 year mortality was 24% in patients with no renal insufficiency, 46% in patients with mild renal insufficiency, and 66% in patients with moderate renal insufficiency (P < 0.001). Therefore renal insufficiency was found to be an independent risk factor for death in elderly patients after MI. Rozic et al. reported that in NSTEMI patients most significant independent early predictor of 30-day mortality was admission heart failure (OR 41.21, 95% CI: 3.520-484.66, P = 0.003), followed by admission serum creatinine (OR 0.989, 95% CI: 0.981-0.997, P = 0.008) and TnT (OR 0.263, 95% CI: 0.080-0.861). Cakar et al. studied the effect of admission creatinine levels on 1-year mortality in acute MI and divided patients in two groups based on serum creatinine levels as elevated group (serum creatinine >1.3 mg/dl) and normal group (serum creatinine <1.2 mg/dl). The mean creatinine level was 1.78 + 7 mg/dl in the elevated group and 0.9 + 0.18 mg/dl in the normal group (P < 0.0001). The mortality rate of the elevated group (n = 7, 25.9%) was higher than that of the normal group (n = 9, 6.8%). A significant increase in 1 year mortality is also observed (P = 0.002).

CrCl was calculated for ACS patients. Mean value of CrCl in STEMI patients was 99.88 + 35.80, in NSTEMI patients was 117.20 + 5.19 and for UA patients, it was 100.89 + 32.80. Smith et al. studied renal impairment in long-term mortality risk prediction after acute MI in 118,753 patients. Mean creatinine was 1.3 + 0.7 mg/dl and CrCl was 55 + 21 m/min. by 10 years, 68% of patients Dhad died.
Compared with normal renal function, even mild renal impairment increased the 10 year risk for mortality by 10%. Severe renal impairment had doubled the risk for mortality at 1 year, and this increased risk persisted at both 5 and 10 year.

The mean value of serum urea in STEMI patients was 72.67 + 59.19, and in NSTEMI patients, it was 39.801 + 11.05, and in UA patients, mean serum urea was 65.78 + 56.97. Serum urea is one of the most frequently determined clinical indices for estimating renal function, it is useful in differential diagnosis of acute renal failure and pre-real condition. Kirtane et al. studied an independent association of elevated BUN for adverse outcome in patients of ACS. They reported a stepwise increase in mortality with increase in BUN in ACS patients independent of the serum creatinine levels. Ostfeld et al. reported that each 1 mg/dl increase in BUN was associated with an average increased odds of having a CAD burden score greater or equal to the 75th percentile of 12% (OR 1.12 (1.05, 1.19 P < 0.01).

Another marker of renal impairment is the serum uric acid. Mean value of serum uric acid in STEMI patients was 4.92 + 1.34, in NSTEMI patients was 4.20 + 1.32, and UA patients, it was 4.48 + 1.37. Nadkar and Jain reported the statically significant higher levels of serum uric acid in MI patients on duty 1 as compared to controls and these levels were more than 7.0 g/dl. Patients who died in 3 days of hospitalization. Chen et al. retrospectively studied uric acid levels in 502 patients of acute STEMI. Higher levels were observed in patients with three vessel disease (330.67 + 2106.47 µmol/L). Hyperuricemia patients with acute MI have a higher rate of left ventricular systolic and diastolic dysfunction including heart failure. Berzein and Kremzer reported serum uric acid as independent marker of coronary calcification in asymptomatic CAD. Timoteo et al. reported that serum uric acid has been a forgotten prognostic marker in ACS. In study of 683 patients, they reported best cut-off of uric acid to predict 1-year mortality of 6.25 mg/dl with sensitivity of 59% and specificity of 72%. In our study, mean values of serum uric acid were higher in patients of STEMI than NSTEMI or UA. Thus, serum uric acid can be taken as an independent predictor of all-cause mortality-term after the whole spectrum of ACS and has an added value for risk stratification. Albuminuria has also been a marker for renal impairment. On urinalysis, 21.1% of STEMI patients had proteinuria of Grade 2 or more. No NSTEMI patient had proteinuria of Grade 2 and above. About 4 (17.4%) UA patients had proteinuria of Grade 2 and more. The more precise risk evaluating factor than proteinuria alone is the ACR. Majority of the patients had ACR <30. Among STEMI patients, 11.1% had ACR in between 500 and 1000, whereas 9.1% had ACR above 1000. In UA patients, only two patients had ACR above 1000. Beton et al. studied the effect of albuminuria in 1-year mortality of MI patients. They reported that at multivariable analysis, the ACR was the strongest among several independent predictors of mortality [adjusted relative risks: 3.6 (95% CI: 2.1-6.2) on the 1st day, 4.9 (95% CI: 2.9-8.2) on the 3rd day and 4.0 (95% CI 2.3-6.8) on the 7th day]. Brantsma et al. in study reported that for each doubling of baseline urinary albumin excretion, the hazard ratio for a CV event was 1.36 (95% confidence interval [CI] 1.31-1.42). Study by Roest et al. in postmenopausal women confirmed the predictive role of urinary albumin for the risk of future cardiovascular mortality independent of hypertension and diabetes. Study by Kweon et al. reported that higher normal ranges of urine ACR are independently associated with carotid intima-media thickness. Sadak et al. reported a direct association between micro-albuminuria and extension of atherosclerotic coronary lesions (P = 0.009). Thus, ACS can be regarded as one of the important and independent risk factor for mortality in ACS patients.

Serum homocystiene was examined in some of the patients. In 10 STEMI patients, the mean value was 31.28 + 7.18 and in two UA patients, it was 37.66 + 7.85. Omland et al. reported that in a multivariate model of predication, serum homocystiene (14.1 µmol/L) was significantly associated with all-cause-mortality (RR 1.78 (95% CI – 1.06 – 2.9)) (P = 0.03).

Thus, study finds that renal parameters studied have important role in prognosis of ACS patients. These factors have an independent risk of mortality and morbidity in ACS patients.

Limitations of the Study
Though the renal dysfunction is reported to be an independent risk factor for morbidity and mortality in ACS patients. Our study had some limitations. The study population was evaluated only at a single visit and no follow-up of patients after the discharge was made to ascertain health status. Data were collected at single point of time. The sample size studied was small and results would be more meaningful with the higher sample size. Thus, a study with large cohort of patients and for longer duration with long-term follow-up is warranted to focus more on risk of ACS in CKD patients in Indian scenario.

CONCLUSION
ACS are among the major causes of morbidity and mortality globally including developing countries like India. Spectrum of ACS incorporates STEMI, NSTEMI, and UA. Risk of developing ACS has been established with risk factors such as smoking, obesity, hypertension,
and diabetes. Renal impairment has also been mortality following ACS. Each renal parameter including serum creatinine, CrCl, serum urea, serum uric acid levels, and urinary ACR has been reported to predict the risk of ACS independently of the other risk factors. Development of ACS in CKD patients complicates the management strategies. In this study, we found that the renal function parameters were deranged in diagnosed patients of ACS. All the parameters described above were deranged in ACS patients who had CKD. The long term morbidity and mortality is higher in those ACS patients who have deranged renal function, incorporating renal function parameters for regular assessment of patients at risk of developing ACS and measuring the renal function parameters in patient who have developed ACS at their first clinical visit in emergency department becomes important for risk stratification. Thus, it is concluded that renal function monitoring must be done in patients at risk or who have developed ACS for reducing the long term morbidity and mortality in such patients.

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World Health Organization; 2011.


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Radiological and Clinical Assessment of Calcaneal Fractures Treated with Open Reduction and Internal Fixation

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Abstract

Introduction: Calcaneal fracture has been one of the most challenging problems facing orthopedic surgeons all around the world as there have been no evidence-based guidelines for the same. This is a retrospective-prospective study to analyze the outcome of the displaced intra-articular fractures of calcaneum treated by open reduction and internal fixation (ORIF).

Materials and Methods: In this study, the outcome of 30 patients was analyzed radiologically by measuring Bohler’s and Gissane’s angle on X-ray and, clinically by American Orthopedic Foot and Ankle Society Hind Foot Scale (AOFAS) and Iowa Calcaneal Score (ICS) results.

Results: In our study, out of 30 subjects, 3 had excellent, 21 had good, and 6 had fair results. 28 subjects had Bohler’s angle more than 10 degrees. 5 patients had superficial wound complications. After statistical analysis, a significant correlation was found between AOFAS and Bohler’s angle ($P < 0.01$), ICS and Bohler’s angle ($P < 0.05$), and no significant correlation was found between Gissane’s angle and AOFAS.

Conclusion: ORIF of calcaneal fracture yield good clinical outcome if Bohler’s angle $>10^\circ$ is achieved, without significant risk of complication.

Key words: Bohler’s angle, Calcaneal fracture, Gissane’s angle

INTRODUCTION

Treating calcaneal fractures have been a controversy as it has not been proved beyond reasonable doubt that surgical intervention alters the eventual outcome of many if not all calcaneal fractures which still continue to be among the most challenging problems facing orthopedic surgeons all around the world. The fatalism with the treatment of intra-articular fractures of calcaneal which existed was described by Cotton and Henderson (1916) and Bankarts (1942). Till very recently, many orthopedic surgeons believed that

“the natural history” of the type of intra-articular fracture and the not “the intervening treatment” determined the final result. The perception was that these comminuted fractures which looked like unintelligible bag of bones on standard X-rays were “inoperable.” Reviews on this subject, however, have failed to demonstrate indisputable superior results of a single approach to the treatment of displaced intra-articular calcaneal fractures. However, with the advent of computer tomography (CT) and with improved methods of internal fixation the understanding, the treatment of these fractures has revolutionized. This is a retrospective-prospective study to assess the results of calcaneal fractures treated with open reduction and internal fixation (ORIF). The patients operated for calcaneum were assessed on the basis of radiological features and clinical outcome of the surgery. The study will also assess if there is any relation in the radiological findings and the subjective outcome.

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MATERIALS AND METHODS

This is a retrospective-prospective analysis of results of 30 patients treated by surgery for displaced intra-articular calcaneal fracture at the Seth GS Medical College, Mumbai, from June 2006 to December 2009 after the Institutional Ethics Committee approval.

All the fractures of the calcaneum were diagnosed on the basis of lateral and axial projection X-rays. Three-dimensional CT scan was done in all of the cases and fractures were classified as per Sanders classification into Type 1 to Type 4.

The inclusion criteria of our study were: (a) Patients presenting with displaced intra-articular fractures of the calcaneus; (b) age 18-65 years inclusive; (c) informed consent obtained. The exclusion criteria were: (a) Medical contraindication; (b) previous calcaneal pathology; (c) previous calcaneal surgery; (d) open calcaneal fracture; (e) injury >21-day-old.

All the patients were on strict limb elevation, crepe bandage application, and ice fomentation till appearance of “positive wrinkle test” which was approximately 7-10 days post injury. The cases of bilateral fracture of calcaneum were operated in single stage. If blisters occurred, the patient was operated after healing of blisters.

With the patient in lateral decubitus position and under tourniquet, lateral approach modified by Benirschke and Sangeorzan was used. A full thickness flap was raised subperiosteally. The peroneal tendons were lifted off in their sheath and subluxated over the fibula. The calcaneofibular ligament was sharply cut off from calcaneum leaving a cuff behind for repair later. Two K-wires were passed into the talus and one into fibula to retract the peroneal tendons and obviated need for manual retraction. Fractured lateral cortex was opened like a trap door; the depressed joint fragment was revealed and elevated against the undersurface of the talus. To facilitate the disimpaction of the fragment, heel was forced into marked varus with pointed clamp applied to tuberosity fragment while the joint reduction the tuberosity is manipulated with thick K-wire to correct varus and superior displacement allowing restoration of Bohler’s angle. After confirmation on X-rays, the fragments are fixed with calcaneal plate and 3.5 or 4 mm screws (Figures 1-3). The wound was closed was a suction drain. Post-operative strict limb elevation was given, antibiotics for 48 h and ankle mobilization was started after 7 days. The patient was mobilized non-weight bearing for 6-8 weeks. After 8-10 weeks, gradual weight bearing is started and full weight bearing allowed within another 4-6 week of time if the patient is comfortable. Follow-up was done at 6 weeks, and at every 3 months thereafter. At the follow-up, lateral and axial views X-rays were taken; and the Bohler’s angle and Gissane angle were looked for.

Clinical results were assessed with Iowa Calcaneal Score (ICS) and American Orthopedic Foot and Ankle Society
Hind Foot Score (AOFAS). The subtalar motion was evaluated accordingly to the method of Morrey and Wideman where heel jog is estimated as percentage of normal. Furthermore, time required for walking full weight bearing was recorded.

RESULTS

In the present series, 30 calcaneal fractures were operated out of which 3 were Sander Type IV, 9 are Type III, and rest 18 were Type II (Table 1). Only 5 were females rest 23 were males.

The study had an average follow-up of 15 months (range 3 months to 5 years).

On clinical assessment with the AOFAS hindfoot score, the average score was 78.7 (range 55-97) and with ICS average was 78.3 (range 50-100). The AOFAS score of 90-100 was considered excellent, 75-89 as good, 50-74 as fair, and <49 as poor outcome. 80% of the patients had good or excellent results. As per Sanders classification, among the 18 Type II fractures, 2 had excellent, 15 had good, and 1 had fair results, whereas in Type III fractures, 1 had excellent, 6 had good, and 2 had fair results. All the 3 Type IV fractures had fair results (Table 2).

The Bohler’s and Gissane’s angles were calculated on follow-up lateral X-rays of calcaneum. The average Bohler’s angle achieved was 24.6 (0-44). The average Gissane’s angle achieved was 120 (100-150). According to statistical analysis (Pearson’s correlation coefficient), there was a significant correlation between Bohler’s angle and AOFAS score \((P < 0.01)\) (Figure 4) and also between ICS and Bohler’s angle \((P < 0.05)\) (Figure 5). There was no significant correlation between Gissane’s angle and AOFAS score (Figures 6 and 7). Table 3 shows the results of this study.

![Figure 4: Relation of Bohler’s angle with American Orthopedic Foot and Ankle Society](image)

![Figure 5: Relation of Bohler’s angle with Iowa calcaneal score](image)

![Figure 6: Relation of Gissane’s angle with American Orthopedic Foot and Ankle Society](image)

Table 1: Type of fracture according to sanders classification

<table>
<thead>
<tr>
<th>Type of fracture</th>
<th>Number of cases (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>II</td>
<td>18 (60)</td>
</tr>
<tr>
<td>III</td>
<td>9 (30)</td>
</tr>
<tr>
<td>IV</td>
<td>3 (10)</td>
</tr>
<tr>
<td>Total</td>
<td>30 (100)</td>
</tr>
</tbody>
</table>

Table 2: Type of fractures and AOFAS in study group

<table>
<thead>
<tr>
<th>Type of fracture</th>
<th>AOFAS&lt;75</th>
<th>AOFAS≥75</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>II</td>
<td>1</td>
<td>17</td>
<td>18</td>
</tr>
<tr>
<td>III</td>
<td>2</td>
<td>7</td>
<td>9</td>
</tr>
<tr>
<td>IV</td>
<td>3</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>Total</td>
<td>6</td>
<td>24</td>
<td>30</td>
</tr>
</tbody>
</table>

\(\chi^2=14.38, \ P<0.001.\) AOFAS: American Orthopedic Foot and Ankle Society
All the 24 cases with excellent and good result had good pain relief. 22 patients walked full weight bearing in 6 months duration, while 6 cases within 9 months due to delayed wound healing or associated injuries. There were 5 cases of post-operative wound dehiscence (Table 4). The dehiscence was at the angle of the incision for 2-3 cm. It was deep till subcutaneous tissue, but plate was not exposed. One patient had low-grade infection in form of sinus and is been treated with oral antibiotics and has been advised plate removal after bony union. None of the patients developed severe infection.

**DISCUSSION**

Calcaneal fractures deserve an aggressive well-planned surgical treatment similar to any other intra-articular fracture. Consistently, better results with surgical treatment have been reported in the recent literature. The meta-analysis done by Randle et al., which studied operative versus non-operative results for calcaneum fracture in the literature, found a trend for operatively treated patients to have better outcomes with respect to pain, return to work, heel width, gait abnormalities, and radiographic outcomes. However, due to small number of subjects, no statistically significant difference was found. In addition, although a statistically significant difference was reported for pain-free walking distance and return to work in two studies, neither of these studies involved random assignment of treatment, allowing for potential selection bias. Thordarson and Krieger performed a randomized, prospective trial comparing operative with non-operative treatment. Follow-up assessment was consistent and, with use of the 100-point scoring system of the AOFAS, the functional score averaged 86.7% for the group that had been treated operatively compared with 55.0% for the group that had been treated non-operatively ($P < 0.0001$).

Table 5 shows analysis of few more articles on treatment of calcaneal fractures.

The result in our series is encouraging because they show an 80% overall excellent to a good outcome with ORIF. In contrast to other authors who recommend the systematic use of a bilateral approach for joint depression fractures, all the fractures could be reduced through an extensile lateral approach.

Among the 18 Type II fractures, 2 had excellent, 15 had good, and 1 had a fair result. The bad result was due to inability to achieve Bohler’s angle intraoperatively.

One of the bad results in Type III fracture may be due to low-grade infection. This patient is advised to remove plate after bony union.

All the 3 Type IV fractures had fair results. In one of them, Bohler’s angle was $>10^\circ$ while, in other two, it is $>10^\circ$, but one of the patients had wound dehiscence.

The incidence of wound infection was in only one of the 30 patients. Five patients had wound dehiscence which readily resolved completely with daily dressing and delayed mobilization, of these, two were Type IV; two were Type III, and one Type II fracture. It is thought.

### Table 3: Results of our study

<table>
<thead>
<tr>
<th>Type of fracture</th>
<th>Number of patients</th>
<th>Excellent results AOFAS&gt;90</th>
<th>Good results AOFAS 75-90</th>
<th>Fair results AOFAS&lt;75</th>
<th>Bohler&gt;10</th>
<th>Bohler&lt;10</th>
</tr>
</thead>
<tbody>
<tr>
<td>II</td>
<td>18</td>
<td>2</td>
<td>15</td>
<td>1</td>
<td>17</td>
<td>1</td>
</tr>
<tr>
<td>III</td>
<td>9</td>
<td>1</td>
<td>6</td>
<td>2</td>
<td>9</td>
<td>0</td>
</tr>
<tr>
<td>IV</td>
<td>3</td>
<td>0</td>
<td>0</td>
<td>3</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>30</td>
<td>3</td>
<td>21</td>
<td>6</td>
<td>28</td>
<td>2</td>
</tr>
</tbody>
</table>

AOFAS: American Orthopedic Foot and Ankle Society

### Table 4: Complication and type of fracture

<table>
<thead>
<tr>
<th>Type of fracture</th>
<th>Delayed wound healing</th>
<th>Low grade infection</th>
<th>Bohler&gt;10</th>
<th>Bohler&lt;10</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>II</td>
<td>2</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>2</td>
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<tr>
<td>III</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>IV</td>
<td>2</td>
<td>0</td>
<td>2</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Total</td>
<td>5</td>
<td>1</td>
<td>5</td>
<td>1</td>
<td>6</td>
</tr>
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</table>

Figure 7: Relation of Gissane’s angle with Iowa calcaneal score
<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Type of study</th>
<th>Duration</th>
<th>Number of fractures</th>
<th>Intervention</th>
<th>Non-operative score</th>
<th>Operative score (a)</th>
<th>Bohler's non-operative</th>
<th>Bohler's post-operative (b)</th>
<th>Score significant</th>
<th>Angle significant</th>
<th>Relation an A and B</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ibrahim et al.</td>
<td>2008</td>
<td>RCT</td>
<td>15 years</td>
<td>26</td>
<td>ORIF</td>
<td>AOFAS=78.5</td>
<td>AOFAS=70</td>
<td>10</td>
<td>16.9</td>
<td>No</td>
<td>(P=0.66)</td>
<td>Yes</td>
<td>Comparable results</td>
</tr>
<tr>
<td>Buckley</td>
<td>2002</td>
<td>RCT</td>
<td>2 years</td>
<td>471</td>
<td>ORIF</td>
<td>sf36=64.7</td>
<td>sf36=68.7</td>
<td></td>
<td></td>
<td>No</td>
<td>(P=0.07)</td>
<td>Yes</td>
<td>Physical therapy without WCB operative results significant better (P=0.001)</td>
</tr>
<tr>
<td>Longino and</td>
<td>2001</td>
<td>RCT</td>
<td></td>
<td></td>
<td>ORIF and BG</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>No</td>
<td></td>
<td>No</td>
<td>Similar to ORIF without BG</td>
</tr>
<tr>
<td>Buckley</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>No</td>
<td></td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>Schepers et al.</td>
<td>2007</td>
<td>Case series</td>
<td>Long term</td>
<td>61</td>
<td>Percutaneous</td>
<td>AOFAS=83</td>
<td></td>
<td></td>
<td></td>
<td>No</td>
<td></td>
<td>No</td>
<td>Percutaneous has good results</td>
</tr>
<tr>
<td>Gavlik et al.</td>
<td>2002</td>
<td>Case series</td>
<td>1 year</td>
<td>10</td>
<td>Arthroscopy and percutaneous fixation</td>
<td>AOFAS=93.7</td>
<td></td>
<td></td>
<td></td>
<td>Yes</td>
<td>(P=0.01)</td>
<td>No</td>
<td>Good results with their technique</td>
</tr>
<tr>
<td>Magnan et al.</td>
<td>2006</td>
<td>Case series</td>
<td></td>
<td>54</td>
<td>Orthofix</td>
<td>MFS</td>
<td>6.98</td>
<td>21.94</td>
<td></td>
<td>Yes</td>
<td>(P=0.01)</td>
<td>No</td>
<td>Similar to ORIF</td>
</tr>
<tr>
<td>Stulik et al.</td>
<td>2006</td>
<td>Case series</td>
<td></td>
<td>287</td>
<td>K-wire</td>
<td>CNS=83.9</td>
<td></td>
<td></td>
<td></td>
<td>No</td>
<td></td>
<td>No</td>
<td>Similar to ORIF</td>
</tr>
<tr>
<td>Wu et al.</td>
<td>2005</td>
<td>Case series</td>
<td>1 ½ years</td>
<td>35</td>
<td>ORIF</td>
<td>AOFAS=88.1 (II), 78.8 (III)</td>
<td>5.6</td>
<td>28.2</td>
<td></td>
<td>No</td>
<td></td>
<td>No</td>
<td>ORIF better</td>
</tr>
<tr>
<td>Li et al.</td>
<td>2008</td>
<td>RCT (K-wire vs. ORIF)</td>
<td>1 year</td>
<td>71</td>
<td>K-wire versus ORIF</td>
<td></td>
<td></td>
<td></td>
<td>Yes</td>
<td></td>
<td>No</td>
<td>Comparable results; less wound problems with K-wire ORIF better</td>
<td></td>
</tr>
<tr>
<td>Laughlin</td>
<td>1996</td>
<td>Case series</td>
<td>2 years</td>
<td>21</td>
<td>ORIF</td>
<td>MFS</td>
<td></td>
<td></td>
<td></td>
<td>No</td>
<td></td>
<td>No</td>
<td>ORIF better, no correlation in Bohler's angle and outcome ORIF better than conservative</td>
</tr>
<tr>
<td>Hutchinson and</td>
<td>1994</td>
<td>Case series</td>
<td>3 years</td>
<td>47</td>
<td>ORIF</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>No</td>
<td></td>
<td>No</td>
<td>ORIF better; correlation in Bohler's angle and outcome</td>
</tr>
<tr>
<td>Huebner</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>No</td>
<td></td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>O’Farrell et al.</td>
<td>1993</td>
<td>RCT</td>
<td>15 months</td>
<td>24</td>
<td>ORIF</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>No</td>
<td></td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>Kennedy et al.</td>
<td>2005</td>
<td>RCT</td>
<td></td>
<td>36</td>
<td>AOFAS, sf-36</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>No</td>
<td></td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>Our study</td>
<td></td>
<td>Case series</td>
<td>15 months</td>
<td>30</td>
<td>ORIF</td>
<td>AOFAS=78.7</td>
<td>24.7</td>
<td></td>
<td></td>
<td>Yes</td>
<td>(P=0.001)</td>
<td>No</td>
<td></td>
</tr>
</tbody>
</table>

RCT: Randomized control trial, ORIF: Open reduction and internal fixation, MFS: Maryland foot score, CNS: Creighton-Nebraska Health Foundation Assessment Score, AOFAS: American Orthopedic Foot and Ankle Society, WCB: Worker’s Compensation Board
that there is thrombosis of the vessels at the anastomosis between lateral peroneal and planter vessels at initial trauma, and internal fixation is thought to jeopardize the already damaged soft-tissue coverage on the lateral side, the incidence of wound complications can be reduced by proper timing and technique of surgery. Because of the small number of patients, it is difficult to correlate achievement of Bohler's angle with wound infection.

Although for some authors bone grafting seems to play an important role, most of the others do not prefer it. In our study, none of the patients required bone grafting.

In our study, we found a significant correlation between Bohler's angle and AOFAS score (\(P < 0.01\)) and Bohler's angle and ICS (\(P < 0.05\)), whereas there was no significant correlation between Gissane's angle and AOFAS.

In 28 fractures, the Bohler's angle was <10° and two had <10°. Both patients where Bohler's angle was <10 had fair results. Similar results were shown by Paul et al. (Table 6).

The bad results in the current study were mainly represented by the three Type IV fracture, one patient of Type II fracture with technical failure to achieve Bohler's angle and two Type III fractures with wound complications.

The shortcomings of this study are its small cohort size, lack of control group, and short follow-up period. Currently, we prefer treating calcaneal fractures with use of rigid calcaneus-specific fixation plates.

### CONCLUSION

In this study, ORIF of calcaneal fractures showed excellent to good results in 80% of the patients. The results are poor as comminution increases. A single lateral extensile approach is sufficient to reduce all fractures. Only one of the 30 fractures had wound infection with this approach. Additional bone graft was not required. Intraoperative achievement of Bohler's angle determines the outcome. Thus, ORIF of fractures of the calcaneum can only be

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Type</th>
<th>Duration</th>
<th>Number of points</th>
<th>Intervention</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Janzen and Douglas</td>
<td>1992</td>
<td>A</td>
<td></td>
<td></td>
<td>ORIF</td>
<td></td>
</tr>
<tr>
<td>Richards and Bridgman</td>
<td>2001</td>
<td>Review</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Paul et al.</td>
<td>2004</td>
<td>case series</td>
<td>6.5 years</td>
<td>70</td>
<td>ORIF</td>
<td></td>
</tr>
</tbody>
</table>
| Loucks and Buckley | 1999 | Prospective cohort study | 2 years | 95               | ORIF versus non-operative | A. Open reduction and internal fixation did successfully increase Bohler's angle, yet this increase in angle did not correlate with improved clinical outcome scores  
B. Those fractures with a marked initial loss of Bohler's angle (<0°) had the worst outcomes. A large initial displacement (increasing energy absorbed), regardless of treatment, resulted in a poorer outcome. This suggests that Bohler's angle has significant prognostic value in terms of predicting long-term morbidity associated with these devastating injuries. |

CT: Computed tomography, ORIF: Open reduction and internal fixation
expected to benefit those patients with nearly anatomical reconstruction. We recommend to open reduce and internally fix the displaced intra-articular fracture of the calcaneum.

REFERENCES

Hematological Changes in Pregnancy-induced Hypertension

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1Assistant Professor, Department of Pathology, BYL Nair Charitable Hospital & TN Medical College, Mumbai, Maharashtra, India,
2Ex-Professor and Head, Department of Pathology, Karnataka Institute of Medical Sciences, Hubli, Karnataka, India

Abstract

Background: Pregnancy-induced hypertension (PIH) is the most common medical disorder of pregnancy contributing significantly to maternal/fetal morbidity and mortality. Hemostatic abnormalities that range from thrombocytopenia, consumption coagulopathy to hemolysis, elevated liver enzymes, and low platelets (HELLP) are the most ominous complications seen. This study was taken to evaluate the nature of these special hematological abnormalities in PIH.

Materials and Methods: A total 200 patients with clinical diagnosis of PIH referred to the department of pathology for hematologic evaluation over a period of 1½ year were included in the study. Complete hemogram, routine urine examination, and aspartate aminotransferase/alanine aminotransferase were done in all patients. Coagulation tests such as prothrombin time activated partial thromboplastin time, thrombin time, and D-dimer were carried out only in patients with thrombocytopenia (platelet count <1.5 lakhs), i.e., on 42 patients.

Results: Around 112 patients were grouped as severe PIH and 88 patients were grouped as mild PIH. Five of the severe PIH patients and only one of the mild PIH patient progressed toward HELLP syndrome. Useful parameters in the hemogram were blood picture to indicate microangiopathic hemolytic anemia, consumption coagulopathy, reticulocytosis, and leukocytosis which helped to identify the need for early initiation of specific therapy. The D-dimer test along with the platelet count was useful in predicting impending disseminated intravascular coagulation. HELLP syndrome with its grave prognosis was identified in 6 patients using blood picture and elevated liver enzymes.

Conclusion: This study shows that repeated hemogram and study of blood smear can go a long way toward identifying patients who are likely to go in for one or the other complications of PIH and identify those requiring specific component therapy by undertaking coagulation studies in a certain percentage of these patients.

Key words: Coagulation, Hemolysis; elevated liver enzymes and low platelets, Pregnancy-induced hypertension, Thrombocytopenia

INTRODUCTION

Pregnancy-induced hypertension (PIH) is the most common disorder of pregnancy affecting approximately 5-7% of pregnancies and is a significant cause of maternal and fetal morbidity and mortality.1 The incidence of PIH in India ranges from 5% to 15%.2 The majority of patients remains in mild to moderate group and does not have any major obstetric problems. However, in a certain proportion of patients, the risk to the mother can be significant and includes the possible development of disseminated intravascular coagulation (DIC), intracranial hemorrhage, renal failure, retinal detachment, pulmonary edema, liver rupture, abruptio placenta, and death. However, in a certain percentage of patients, the disease can progress to a more severe form with maternal risk of convulsions, cerebrovascular accidents, or increasing morbidity. For the fetus, it is also associated with placental insufficiency, intrauterine growth retardation, and rarely even intrauterine device.3

Hemostatic abnormalities ranging from thrombocytopenia, consumption coagulopathy to the triad of hemolysis, elevated liver enzymes, and low platelets (HELLP) are
the more ominous complications seen in severe PIH. Thrombocytopenia is the most common hemostatic abnormality and its detection is important as it is one of the preventable factors contributing to some cases of life threatening cerebral and hepatic hemorrhage. In view of the magnitude of coagulation changes that occurs in normal pregnancy, it is not surprising that pregnant or puerperal patient develops overt thromboembolic or coagulation abnormalities. It is equally reasonable to explore whether more subtle coagulation fibrinolytic changes develop into patterns of pathologic significance in diseases unique to pregnancy like toxemia.

Superimposed HELLP syndrome develops in 4-12% of women with pre-eclampsia or eclampsia. HELLP syndrome is severe form of pre-eclampsia, which poses a significant threat to both mother and fetus. This acronym HELLP was first coined by Weinstein, in 1982, to emphasize the triad of hemolysis, elevated liver, and low platelets. Based on the lowest observed maternal platelet count, HELLP syndrome is classified into three classes: Class 1 - If platelet count <50,000/cumm, Class 2 - If platelet count is 50,000 and <100,000/cumm, and Class 3 - If platelet count >100,000 and <150,000/cumm.

Pathophysiological, it is characterized by microangiopathic hemolytic anemia associated with liver and kidney damage that can progress to DIC having fatal termination.

This study was taken up to evaluate the nature of these hematological abnormalities in PIH. Evaluation of peripheral smear with a special reference to red blood cell morphology, platelet morphology, aggregation and number has been the important focus of the study. Abnormal and premature forms of erythrocytes can identify microangiopathic hemolytic anemia cases which can progress to levels which require aggressive therapy. Cases having platelet counts below 1.5 lakhs were selected for performing battery of coagulation tests. Special emphasis was laid on D-dimer testing which can be used as a sensitive screening and follow-up tool for pre-eclamptic coagulopathy helping to define a subset of patients with severe disease. The D-dimer testing has been preferred over the test for fibrin degradation products (FDPs) as it has been established as a more sensitive tool for fibrinolysis.

MATERIALS AND METHODS

This was a prospective study carried out over a period of 1½ years at the Department of Pathology, Karnataka Institute of Medical Sciences, Hubli, a major tertiary health center for Karnataka. The total cases attending the outpatient department (OPD) per year are 3.5 lakhs of which around 15,000 cases attend antenatal OPD. Average number of antenatal cases admitted for delivery is 7000 per year of which about 450 cases are diagnosed to be having PIH.

About 200 patients diagnosed with PIH admitted to antenatal ward of KIMS and referred to the pathology department for hematological studies over a period of 1½ year were evaluated. Patients with essential hypertension, malnutrition, sepsis, neoplastic diseases, chronic diseases, valvular heart diseases, and those on anticoagulants were excluded. Clinical examination, complete hemogram, bleeding time, urine examination, and liver function tests were done on all the patients (200 patients).

Coagulation tests of prothrombin time (PT), activated partial thromboplastin time (APTT), thrombin time (TT), and D-dimer were done only on patients with platelet count below 1.5 lakhs (42 patients).

After obtaining informed consent from all the patients, venous blood was collected using 21G disposable needle and disposable plastic syringe. 4 cc of blood was collected for complete hemogram, of which, 2 cc of blood was collected in ethylenediaminetetra-acetic acid bulb for determination of hemoglobin (Hb), red cell indices, packed cell volume, total count, and platelet count. This was determined using Sysmex K-1000 automated blood cell counter. The remaining 2 cc of blood was collected in a citrate bulb for estimation of erythrocyte sedimentation rate (ESR) by Westergren’s method. One drop of blood was obtained by finger prick for preparing peripheral smear and stained by Wrights stain. Bleeding time was estimated by Ivy’s method. In those cases, where coagulation tests were done an additional 1.8 cc of venous blood was collected in citrate bulb mixed with 0.2 ml of citrate and used for coagulation studies.

The reagent used for PT was liquiplastin (Tulip Diagnostics). Normal values using liquiplastin are between 10 and 14 s. For each lot of liquiplastin, the mean normal PT was established by taking plasma from 20 normal healthy individuals and obtaining the average of their PT values.

The reagent used for APTT was liquicel in (Tulip Diagnostics), and the normal value is 21-29 s. Controls were run simultaneously with each test using plasma from healthy individuals.

The reagent used for TT was Fibroscreen (Tulip Diagnostics). Normal values using this reagent are formation of solid gel clot in 5-15 s.

D-dimer was estimated using Tulip XL FDP. Quantification was done by preparing serial dilutions of plasma sample...
using phosphate-buffered saline buffer solution − 1:2, 1:4, 1:8, 1:16, 1:32, and so on. Positive result was indicated by agglutination indicating a D-dimer level above 200 ng/ml. The absence of agglutination indicates a negative result. D-dimer levels in ng/ml were calculated using the formula:

\[200 \times d\]

Where, \(d\) = Highest dilution of plasma showing agglutination during quantitative test of the sample.

**Statistical Analysis**

Students \(t\)-test was used.

**RESULTS**

Of the 200 cases, 112 (56%) had severe PIH (diastolic blood pressure (BP) ≥110 mmHg) and 88 cases (44%) had mild PIH (diastolic BP ≤100 mmHg). Table 1 shows age distribution of PIH cases.

The mean age in mild PIH was 23.57 ± 3.76 and that in severe PIH was 23.49 ± 4.1. Of the 200 cases, 109 (54.5%) were primigravidas and 91 (45.5%) were multigravidas. Cases with mild PIH were asymptomatic, whereas all cases of severe PIH were symptomatic with headache being the predominant symptom present in 52 cases (46.43%) followed by epigastric pain in 21 (18.75%), blurring of vision in 8 (7.14%), reduced urine output in 6 (5.35%), vomiting in 8 (7.14%), and giddiness in 3 (2.68%) cases. Biochemical examination revealed 1+ proteinuria in 43 cases (48.86%) of mild PIH while majority (55 cases, 49.10%) of those with severe PIH had 3+ proteinuria. Serum bilirubin levels were raised in 1 case (1.14%) of mild PIH and 9 (8.04%) of severe PIH and was normal in the remaining cases. The mean serum bilirubin in the cases with HELLP was as shown in Table 2. The highest level of serum bilirubin of 13.5 mg/dl was seen in a case of HELLP, the range being 1.3-13.5 mg/dl.

Aspartate aminotransferase (AST) levels were slightly elevated (41-70 IU/L) in 3 cases (3.40%) of mild PIH and 28 cases (25%) of severe PIH. Mean AST in cases with HELLP was high as shown in Table 3. Alanine aminotransferase levels were markedly elevated (>70 IU/L) in 9 cases (8.04%) of severe PIH. Hb levels of all these 200 patients varied from 2.3 to 14.8 g%, the mean being 9.05 g%. ESR of these patients ranged from 5 to 170 mm/h. The mean corpuscular volume in mild PIH was 82.91 ± 10.35 and, in severe PIH, it was 81.21 ± 10.26. The mean corpuscular hemoglobin (MCH) in mild PIH was 23.83 ± 6.11 and, in severe PIH, it was 24.13 ± 4.63. The mean MCH concentration in mild PIH was 28.35 ± 5.21 and, in severe PIH, it was 29.30 ± 3.88. Total leukocyte count varied from 4000 to 43,000 cells/cumm. The reticulocyte count varied between 0.5% and 10%. It was raised (>2.5%) in 18 cases (20.45%) of mild PIH and 40 (35.71%) of severe PIH.

Platelet count was normal (>1.5 lakhs) in 81 cases (92.05%) of mild PIH and 77 (86.75%) of severe PIH. Platelet count was between 1 and 1.5 lakhs in 3 cases (3.40%) of mild PIH and in 10 (8.93%) of severe PIH. The count was between 50,000 and 1 lakh in 4 cases (4.55%) of mild PIH and 20 (17.86%) of severe PIH. Platelet count was below 50,000 in 5 cases (4.46%) of severe PIH, whereas in none of those with mild PIH. Bleeding time was prolonged (>6 min) in one case (1.14%) of mild PIH and 10 (8.93%) of severe PIH. 13 cases (11.60%) of severe PIH showed giant platelets in the peripheral smear. Table 4 shows the red cell morphology in mild and severe PIH.

Coagulation tests were done in only those who had platelet count below 1.5 lakhs/cumm, i.e. in 42 cases. 2 cases (28.57%) of mild PIH and 29 (82.86%) of severe PIH had prolonged PT (>14 s). The PT in severe PIH was significantly prolonged (\(P < 0.05\)). APTT was normal in all 7 cases of mild PIH and 27 cases of severe PIH but prolonged (>29 s) in 8 cases (22.86%) of severe PIH.

<table>
<thead>
<tr>
<th>Age group (years)</th>
<th>Mild PIH</th>
<th>Severe PIH</th>
</tr>
</thead>
<tbody>
<tr>
<td>15-20</td>
<td>13 (14.77)</td>
<td>16 (14.29)</td>
</tr>
<tr>
<td>20-25</td>
<td>34 (38.64)</td>
<td>51 (45.53)</td>
</tr>
<tr>
<td>25-30</td>
<td>35 (39.77)</td>
<td>35 (31.25)</td>
</tr>
<tr>
<td>30-35</td>
<td>04 (4.55)</td>
<td>06 (5.36)</td>
</tr>
<tr>
<td>35-40</td>
<td>02 (2.27)</td>
<td>04 (3.57)</td>
</tr>
<tr>
<td>Total</td>
<td>88 (100)</td>
<td>112 (100)</td>
</tr>
</tbody>
</table>

*PIH: Pregnancy-induced hypertension*

<table>
<thead>
<tr>
<th>Patients groups</th>
<th>Mean±SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>HELLP</td>
<td>3.53±4.88</td>
</tr>
<tr>
<td>Non-HELLP</td>
<td>0.72±0.18</td>
</tr>
</tbody>
</table>

*SD: Standard deviation, HELLP: Hemolysis, elevated liver enzymes, and low platelets*

<table>
<thead>
<tr>
<th>Patients groups</th>
<th>Mean±SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>HELLP</td>
<td>253.83±196.33</td>
</tr>
<tr>
<td>Non-HELLP</td>
<td>34.35±16.09</td>
</tr>
</tbody>
</table>

*SD: Standard deviation, HELLP: Hemolysis, elevated liver enzymes, and low platelets, AST: Aspartate aminotransferase*
APTT was not significantly prolonged in severe PIH ($P > 0.05$). The TT was normal in 6 cases (85.7%) of mild PIH and 28 (80%) of severe PIH. TT was raised (>15 s) in 1 case (14.29%) of mild PIH and 7 (20%) of severe PIH. The TT in severe PIH was significantly prolonged ($P < 0.05$).

D-dimer levels in cases of mild and severe PIH are shown in Table 5. In the present study, HELLP syndrome was diagnosed in six patients based on the hematological parameters, blood smear examination, and liver function tests.

**Table 6 shows hematological parameters, coagulation profile, liver enzymes, and outcome in 6 cases of HELLP syndrome.** In this study, 2 cases belonged to Class 1 HELLP syndrome and they had prolonged PT and APTT with TT on the higher side and marked increase in D-dimer levels indicating a state of DIC. Remaining 4 cases belonged to Class 2 HELLP and none of them belonged to Class 3. Four cases with HELLP syndrome underwent cesarean section. One patient died after cesarean and all the 6 patients delivered low birth weight babies.

**DISCUSSION**

Women with severe pre-eclampsia develop a variety of hematologic aberrations which have an impact on the outcome of these patients so that aggressive therapy can be initiated to prevent maternal and neonatal morbidity and mortality. Simple investigations such as complete hemogram, urine examination, and liver enzymes were done on all the cases that can detect platelet abnormalities, red cell abnormality, and detect patients likely to progress to HELLP syndrome. Coagulation profile was done only on patients with thrombocytopenia which is an important parameter for detecting DIC.

Women at any age are said to be at a greater risk for PIH. In the present study, the mean age in mild PIH was 23.57 ± 3.76 and, in severe PIH, it was 23.49 ± 4.1. Similar observation was made by O'Brien et al., who reported a mean age of 21.5 ± 0.9 in mild PIH and 21.3 ± 1.4 in severe PIH.

**PIH:** Pregnancy-induced hypertension

<table>
<thead>
<tr>
<th>RBC morphology</th>
<th>Mild PIH</th>
<th>Severe PIH</th>
</tr>
</thead>
<tbody>
<tr>
<td>N (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normocytic normochromic</td>
<td>38 (43.18)</td>
<td>39 (34.82)</td>
</tr>
<tr>
<td>Dimorphic</td>
<td>16 (18.18)</td>
<td>24 (21.43)</td>
</tr>
<tr>
<td>Normocytic hypochromic</td>
<td>15 (17.05)</td>
<td>18 (16.07)</td>
</tr>
<tr>
<td>Microcytic hypochromic</td>
<td>13 (14.77)</td>
<td>17 (15.18)</td>
</tr>
<tr>
<td>Macrocytic</td>
<td>03 (3.40)</td>
<td>08 (7.15)</td>
</tr>
<tr>
<td>Microangiopathic hemolytic</td>
<td>01 (1.14)</td>
<td>05 (4.46)</td>
</tr>
<tr>
<td>Leukoerythroblastic</td>
<td>01 (1.14)</td>
<td>01 (0.89)</td>
</tr>
<tr>
<td>Megaloblastic</td>
<td>01 (1.14)</td>
<td>00 (0.0)</td>
</tr>
<tr>
<td>Total</td>
<td>88 (100)</td>
<td>112 (100)</td>
</tr>
</tbody>
</table>

**Table 5: D-dimer levels in mild and severe PIH**

<table>
<thead>
<tr>
<th>D-dimer (ng/ml)</th>
<th>Number of cases (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mild PIH</td>
</tr>
<tr>
<td>Undetectable</td>
<td>4 (57.14)</td>
</tr>
<tr>
<td>200</td>
<td>2 (28.50)</td>
</tr>
<tr>
<td>&gt;200</td>
<td>1 (14.2)</td>
</tr>
<tr>
<td>Total</td>
<td>7 (100)</td>
</tr>
</tbody>
</table>

**Table 4: Red cell morphology in mild and severe PIH cases**

<table>
<thead>
<tr>
<th>RBC morphology</th>
<th>Mild PIH</th>
<th>Severe PIH</th>
</tr>
</thead>
<tbody>
<tr>
<td>N (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normocytic normochromic</td>
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<td>01 (0.89)</td>
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<tr>
<td>Megaloblastic</td>
<td>01 (1.14)</td>
<td>00 (0.0)</td>
</tr>
<tr>
<td>Total</td>
<td>88 (100)</td>
<td>112 (100)</td>
</tr>
</tbody>
</table>

**Table 6: Hematological parameters, coagulation profile, liver enzymes, and outcome in 6 cases of HELLP syndrome**

<table>
<thead>
<tr>
<th>Tests</th>
<th>Case 1</th>
<th>Case 2</th>
<th>Case 3</th>
<th>Case 4</th>
<th>Case 5</th>
<th>Case 6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb (g%)</td>
<td>3.4</td>
<td>4.3</td>
<td>3.6</td>
<td>6.1</td>
<td>3.9</td>
<td>3.5</td>
</tr>
<tr>
<td>Total leukocyte count</td>
<td>8190</td>
<td>20,000</td>
<td>15,000</td>
<td>26,000</td>
<td>9900</td>
<td>4000</td>
</tr>
<tr>
<td>ESR (mm/h)</td>
<td>110</td>
<td>105</td>
<td>120</td>
<td>85</td>
<td>66</td>
<td>112</td>
</tr>
<tr>
<td>Reticulocyte count (%)</td>
<td>2.5</td>
<td>6</td>
<td>8</td>
<td>6</td>
<td>8</td>
<td>8</td>
</tr>
<tr>
<td>Platelet count (lakhs/cumm)</td>
<td>0.80</td>
<td>0.92</td>
<td>0.90</td>
<td>0.88</td>
<td>0.28</td>
<td>0.40</td>
</tr>
<tr>
<td>Bleeding time (min)</td>
<td>6’48&quot;</td>
<td>6’40&quot;</td>
<td>3’40&quot;</td>
<td>3’50&quot;</td>
<td>7’45&quot;</td>
<td>7’40&quot;</td>
</tr>
<tr>
<td>PT (s)</td>
<td>13.6</td>
<td>14.6</td>
<td>16</td>
<td>16.8</td>
<td>16</td>
<td>16</td>
</tr>
<tr>
<td>APTT (s)</td>
<td>28</td>
<td>25</td>
<td>30</td>
<td>26</td>
<td>32</td>
<td>24</td>
</tr>
<tr>
<td>TT (s)</td>
<td>10</td>
<td>13.6</td>
<td>16.2</td>
<td>16</td>
<td>14.8</td>
<td>16</td>
</tr>
<tr>
<td>D-dimer (ng/ml)</td>
<td>200</td>
<td>200</td>
<td>400</td>
<td>400</td>
<td>600</td>
<td>800</td>
</tr>
<tr>
<td>Serum bilirubin (md/dl)</td>
<td>1.3</td>
<td>1.8</td>
<td>1.9</td>
<td>13.5</td>
<td>1.4</td>
<td>1.3</td>
</tr>
<tr>
<td>AST (IU/L)</td>
<td>90</td>
<td>518</td>
<td>380</td>
<td>265</td>
<td>120</td>
<td>90</td>
</tr>
<tr>
<td>ALT (IU/L)</td>
<td>48</td>
<td>488</td>
<td>246</td>
<td>376</td>
<td>98</td>
<td>48</td>
</tr>
<tr>
<td>Mode of delivery</td>
<td>Vaginal</td>
<td>Cesarean</td>
<td>Cesarean</td>
<td>Cesarean</td>
<td>Cesarean</td>
<td>Vaginal</td>
</tr>
<tr>
<td>Birth weight (kg)</td>
<td>2.2</td>
<td>2.1</td>
<td>2.2</td>
<td>2.3</td>
<td>2.3</td>
<td>2.1</td>
</tr>
</tbody>
</table>

Proteinuria is an important sign of pre-eclampsia and diagnosis of pre-eclampsia is doubtful in its absence. In our study, proteinuria was present in all the cases (100%) of mild and severe PIH. However, Jambhulkar et al. observed proteinuria in only 68% cases of mild PIH and 92% cases of severe PIH.11

Estimation of serum bilirubin is important as it not only forms important criteria for diagnosis of HELLP syndrome but also its rise signifies the severity of the condition. Entman et al. in their study reported mean bilirubin concentration in severe PIH to be significantly higher than that in mild PIH.12 However, in our study, there was no significant difference in mean bilirubin concentration between the mild and severe PIH groups. Serum AST appears to be the dominant transaminase released into the peripheral circulation with severe pre-eclampsia and HELLP syndrome. In the present study, the mean AST was higher in HELLP cases compared to non-HELLP cases which was similar to the observation made by de Boer et al.13

The present study showed raised ESR in most of the patients (85%). This is explained by the fact that pregnancy is one of the physiological causes of raised ESR and infection was ruled out in all these patients. Patients with severe pre-eclampsia have a microangiopathic hemolytic anemia, but it is not known whether increased red cell turnover occurs with milder form of this syndrome. Although hemolytic peripheral blood picture was present in only six cases, 18 (20.45%) of mild PIH and 40 (35.71%) of severe PIH showed raised reticulocyte counts (>2.5%). The highest value recorded was 10% in severe PIH with microangiopathic hemolytic anemia. Thrombocytopenia is the most common hemostatic abnormality of pre-eclampsia seen in approximately 50% of patients with pre-eclampsia according to a recent study done by Donimath et al.14 In the present study, 22.5% patients had thrombocytopenia. Thomas et al. in their study observed that 16% of their patients had thrombocytopenia. Kelton et al. in his study concluded that there is evidence of both in vivo and in vitro platelet functional defect as the patients had disproportionate prolongation of bleeding time. Thus, patients with pre-eclampsia can have a significant defect in platelet function as well as number. The bleeding time may be important for evaluation of pre-eclamptic patients and provide information about the risk of any surgical procedures. In the present study, only 5.5% of patients had prolonged bleeding time, whereas in the study by Kelton et al., 34.6% patients with PIH had prolonged bleeding time.13

Microangiopathic hemolytic anemia is present to some degree in all patients with HELLP syndrome. This diagnosis is confirmed by finding of burr cells, schistocytes, and polychromasia on peripheral smear.4 In the present study, six cases revealed these findings. All these six cases had thrombocytopenia and elevated liver enzymes. Documentation of HELLP syndrome is essential as aggressive therapy is initiated to prevent neonatal morbidity and mortality.

It is impossible to say which part of the maternal pathology reflects the HELLP syndrome. The associated DIC is an important aggravating factor often leading to deterioration of maternal status. The diffuse organ system damage particularly in liver, lungs, kidney, and brain may be a direct consequence of DIC causing vessel wall damage and increased vascular permeability. Arterial and venous macro and microthrombosis producing tissue hypoxia and ischemic necrosis. Hence, coagulation test is important in these patients and can reduce maternal morbidity and mortality if delivery is expedited as soon as diagnosis of suspected DIC is made.6,16

The reported hematologic findings in toxemia of thrombocytopenia, hemolysis, increased platelet adhesiveness, and increased FDPs are indicators compatible with intravascular coagulation. In the present study, an attempt was made to determine if the clinical categories of toxemia of pregnancy could be related to the syndromes of DIC on the basis of plasma assays of PT, APTT, and D-dimer estimation. Leduc et al. in their study concluded that DIC occurs once severe thrombocytopenia is present. Hence, one needs to obtain a complete blood count with platelet count at admission followed by serial platelet counts. Evaluation of PT, APTT, and fibrinogen should be added only if platelet count is <1 lakh in pre-eclampsia. This also saves the cost.17 In this study, coagulation studies were done in patients with platelet count below 1.5 lakhs and showed that the mean PT was significantly prolonged in cases with severe PIH. Similar observation was made by Thomas et al. The prolongation of PT reflects picture of utilization of clotting factors due to mild intravascular coagulation. There were no significant differences between the mean APTT of mild and severe PIH patients in this study. However, the mean APTT in severe PIH was significantly prolonged in the study by Thomas et al. and Jambhulkar et al.5,11 Significant prolongation of PTT in severe PIH indicates consumption of coagulation factors, especially factor VIII. In the present study, absence of prolongation of APTT could not be explained. TT was significantly prolonged in our study and similar observation was made by Jambhulkar et al.11 Prolonged TT is ascribed to low concentration of substrate for thrombin, i.e., hypofibrinogenemia.

Coagulation abnormalities are considered one of the more ominous maternal complications in pre-eclampsia.
Unfortunately, there is no sensitive, reliable cost-effective screening tool to detect this and usually a battery of tests such as platelet count, PT, APTT, fibrinogen, and FDP are performed. None of these consistently reflect coagulation abnormalities such as D-dimer test. Although detection of degradation products traditionally has been used to assess fibrin formation, most of these assays cannot actually distinguish whether the products origin is fibrin or fibrinogen and, therefore, not specific for coagulation. The dimeric fragments on the other hand being unique to the process of fibrin polymerization specifically reflects its formation and breakdown. Hence, in the present study, D-dimer was done rather than FDP. D-dimer was detectable, and it was above 200 ng/ml in 1 case of mild PIH and 10 of severe PIH in our study. We observed that D-dimer positive women had greater risk of cesarean section, premature delivery, and low birth weight. Similar observation was made by Trofatter et al. in their study.

Testing for D-dimer may be useful in early screening and follow-up for coagulopathy in PIH and may also help to define the subset of patients with severe disease. D-dimer was also a better indicator of DIC compared to all other tests and correlated well with the outcome of pregnancy in the present study.

CONCLUSION

This study gives an outline of the investigation to be done in cases of PIH which can alert the physician of the severity of the disease so that appropriate and timely management can be initiated. Further, it proves the importance of peripheral blood smear examination which is a very simple and cost-effective tool and can detect the red cell abnormalities and qualitative and quantitative abnormalities of platelets frequently seen in PIH. Coagulation tests can be added only once there is thrombocytopenia, as increased platelet consumption is an early feature of this disorder. This also reduces the expenses of investigations. The importance of liver enzymes is furthermore emphasized, especially in patients with thrombocytopenia to detect HELLP syndrome.

REFERENCES

Comparison of Surgical Outcome in Children with Cochlear Implant Placed using Different Approach

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Abstract

Background: To demonstrate whether there are differences in the outcome of children with cochlear implantation (CI) using the techniques between mastoidectomy with posterior-tympanotomy approach (MPTA) and veria, suprameatal approach (SMA).

Materials and Methods: A study was undertaken of congenitally deaf 43 children (28 boys and 15 girls), who underwent CI before the age of 7 years at a tertiary hospital affiliated to Barkatullah University in Bhopal from 2013 to 2015, were included in this study. All children were profoundly deaf, and radiological assessment was undertaken using magnetic resonance imaging. Children with severe mental retardation, cardiac problem or with cochlear malformations were excluded from the study.

Results: All 43 children had a completely patent cochlea. 30 patients underwent cochleostomy and 13 patients had round window insertion. Full insertion was accomplished in 43 children. In 12 children ALPS implant with 22 channel electrode used and in rest of 31 children's NUCLEUS 22 channeled electrode is used one child developed flap necrosis and two had infected stitches both were treated accordingly and both recovered fully. During follow-up rest, all children did not encounter problems. All children's still wears the cochlear implant showing substantial progress in auditory perception skills. No children experienced device migration or dislodgment of the electrode array.

Conclusion: A surgical outcome of CI in all patients with good early results of tuning and rehabilitation with no significant difference between MPTA techniques and SMA technique.

Key words: Cochlear implant, Mastoidectomy, Suprameatal approach

INTRODUCTION

Congenital sensorineural hearing loss is a significant childhood condition with an incidence in the order of 2/1000 live births. There is significant socioeconomic impact in untreated hearing loss with respect to both school and future employment opportunities.¹

The rate of hearing loss in children has been estimated as 2-3/1000. This includes those cases of genetic hearing loss that present later in childhood or hearing the loss of an acquired etiology.

The advent of neonatal hearing screening has significantly increased early detection of significant childhood hearing loss and resulted in earlier intervention with respect to both hearing amplification and cochlear implantation (CI). Normal hearing is a pre-requisite for adequate speech and language development, and therefore, identification and management of hearing loss is critical to ensure an optimal outcome in this regard.²

CI has provided a major advance in the treatment of children with severe to profound bilateral sensorineural hearing loss. It continues to provide the only real electro/electro-acoustic hearing rehabilitation when hearing aids are no longer useful. Early identification, intervention, and rehabilitation often result in children with significant hearing loss achieving educational and occupational level commensurate with their normal hearing peers. This results in a significant social dividend with respect to education and employment as well as reducing the impact of a hearing disability.³
The conventional technique for CI is the mastoidectomy with posterior-tympanotomy approach (MPTA). Posterior-tympanotomy was first described by Jansen in 1957 as a means of approaching the middle ear. This approach was subsequently embraced by the cochlear implant surgeons as the accepted route of access to the round window and promontory. MPTA for cochlear implant surgery was first introduced by House in 1961. Although it may be relatively easily performed, there have been reports in the literature describing temporary injury to both the facial and chorda tympani nerve. Only a few alternatives to this classical approach have been described in the literature.  

In 2000, Kiratzidis described a technique using a tunnel drilled in the mastoid area without mastoidectomy to approach the middle ear. The endomeatal approach was given in one of the studies but infection and electrode extrusion through the skin of the external auditory canal led to the abandonment of this approach. Collins et al. described an approach via the middle fossa, and Singh used the canal wall down technique in the cases of congenital anomalies. 

The MPTA technique has proven to be efficient for the vast majority of cases; however, one major drawback of this technique is the possibility that the chorda tympani may be sacrificed and/or that the facial nerve may be injured. In the early days of CI, incidences of injury to the chorda tympani and facial nerve of 1.7-2.0% were not uncommon. Although there has been a decline in the incidence of injury to the chorda tympani and facial nerve in recent years, it still occurs on rare occasions.

Several surgical techniques have been described in literature as alternatives to overcome the risk of facial nerve injury. Alternative techniques for CI includes:

1. The endomeatal approach
2. The middle fossa approach
3. The mastoid tunnel technique
4. The pericanal electrode insertion technique
5. The suprameatal technique.

Along with the reduced risk of facial injury, all these alternative techniques have in common that mastoidectomy is avoided. The supra meatal technique introduced by Kronenberg et al. in 1999 seems to be gaining popularity among ear surgeons. It involves exposing the middle ear through the external auditory canal and inserting electrodes into the cochlea through a suprameatal tunnel bypassing the mastoid cavity. This technique is suitable for both children and adults. In addition, extrusion of the electrode through the skin of the external auditory canal is avoided using the suprameatal tunnel.

The suprameatal approach was developed as an alternative technique to the classical approach and it is based on retroauricular tympanotomy approach as access to the middle ear and cochleostomy site. The electrode is introduced into the middle ear via a suprameatal route thus avoiding mastoidectomy.

**MATERIALS AND METHODS**

A study was undertaken of congenitally deaf 43 children (28 boy and 15 girls), who underwent CI before the age of 7 years at a tertiary hospital affiliated to Barkatullah University, Bhopal from 2013 to 2015, were included in this study. All children were profoundly deaf, and radiological assessment was undertaken using magnetic resonance imaging. Children with severe mental retardation, cardiac problem or with cochlear malformations were excluded. 17 patients were operated via supra meatal approach (SMA) approach and 26 patients via posterior-tympanotomy approach. All children were assessed before surgery and 3, 6, 9 and 12 months after surgery. Pre-implant evaluation consisted of pure tone audiometry and tests of speech recognition, both with hearing aid and without hearing aid.

Post-implant evaluation included the same tests with CI off and on, carried out with free field stimulation in a sound proof room. Threshold evaluation was conducted using category of auditory perception, free field stimulation, and in the analyses of speech perception; we considered the speech intelligibility rating and listening skills development rating. In this study, we considered the speech detection threshold (SDT) and speech recognition threshold (SRT). SDT corresponds to the value of sound intensity at which the verbal message is not understood but perceived as generic sound, therefore with a percentage of intelligibility of 0%. The SRT indicates the level of intensity at which the patient correctly repeats 50% of the words.

The surgical outcome looked at the presence of any medical or surgical complication related to the implant surgery or to the age of these patients.

**Surgical Techniques**

The MPTA technique for CI was performed as described by Clark et al. in 1979. It includes mastoidectomy with posterior-tympanotomy and facial reassess approach.

**The SMA Technique Involve**

The middle ear cavity is entered via an endaural tympanotomy after performing a retroauricular incision. A suprameatal tunnel is drilled superoposterior to the suprameatal spina...
toward the posterior part of the aditus-ad-antrum at 1 O’clock position for the left ear and 11 O’clock for the right ear. A bony sub periosteal well is created posteriorly in temporal bone to accommodate the receiver-stimulator and loop of electrode. The electrode is inserted into the cochleostomy, which is drilled anteroinferior to the oval window and give access to scala tympani.

RESULTS

All 43 children had a completely patent cochlea. 30 patients underwent cochleostomy and 13 patients had round window insertion. Full insertion was accomplished in 43 children. In 12 children, ALPS implant with 22 channel electrode used and in rest of 31 children’s NUCLEUS 22 channeled electrode is used one child developed flap necrosis and two had infected stitches both were treated accordingly and both recovered fully. During follow-up rest, all children did not encounter problems. All children’s still wears the cochlear implant showing substantial progress in auditory perception skills. No children experienced device migration or dislodgment of the electrode array.

DISCUSSION

In the hospital where the study was performed 43 patients were operated by Dr. Hans, Dr. Kirtane, and Dr. Haital have operated all cases, and authors have assisted them all cases as the first assistant. Dr. Hans has operated all cases via VERIA Technique while Dr. Kirtane Sir and Dr. Haital have operated via post-tympanotomy technique.\textsuperscript{15-17}

Intraoperative

Neural response telemetry (NRT) was done by other surgical assistants. Intraoperative insertion and functional status of electrode channels are verified by NRT.

All the children were followed for 9 months post-operatively to watch for any surgical complication or difference in results, but all children were found to be normal and having the same surgical outcome.

Post-operative X-ray

Post-operative X-ray is carried out to verify the position of the electrode and to rule out any dislocation/displacement.

Complication

One patient male had flap necrosis (MPTA technique) and two patients had initial stitch infection.

Prognosis

All patients recovered fully.

CONCLUSION

This study shows the same surgical outcome of CI in all patients with good early results of tuning and rehabilitation with no significant difference between MPTA techniques and SMA technique. All 43 children have their implant in position and working perfectly. No patient had any complaint of displacement of the implant of malfunctioning of any electrodes. No difference is seen in surgical outcome in any children underwent surgery via both techniques.

REFERENCES


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Comparative Evaluation of Pre-operative Intramuscular Ephedrine Hydrochloride and Mephentermine Sulfate for Reduction of Spinal Anesthesia-induced Hypotension during Cesarean Section - A Clinical Study

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Abstract

Background: Ephedrine has potent alpha and weak beta stimulatory effects. Due to its alpha receptor affect, it increases heart rate (HR) and cardiac output.

Aims and Objectives: To evaluate and compare the effects of intramuscular (IM) ephedrine hydrochloride and mephentermine sulfate for reduction of spinal anesthesia-induced hypotension in lower segment cesarean section (LSCS).

Materials and Methods: After taking informed consent, 90 healthy full-term pregnant female patients of age 20-35 years of American Society of Anesthesiologists Grade I and II, posted for elective LSCS under spinal anesthesia were included in the study. They were randomly divided into 3 groups of 30 patients each. Patients of Group I - receiving 1 ml injection normal saline intramuscularly 5 min before giving spinal anesthesia; patients of Group II receiving 30 mg injection mephentermine sulfate intramuscularly 5 min before giving spinal anesthesia; patients of Group III - receiving 30 mg injection ephedrine hydrochloride intramuscularly 5 min before giving spinal anesthesia. After giving spinal anesthesia, observation was made for HR, systolic blood pressor, diastolic blood pressor, and SPO₂ at every 2 min interval for first 20 min and then every 5 min up to 1 h. Apgar score was recorded at 1 min and 5 min after delivery.

Results: We found that both ephedrine hydrochloride and mephentermine sulfate given intramuscularly before spinal anesthesia decreases the incidence of spinal anesthesia-induced hypotension. Apgar score was lower in mephentermine sulfate group.

Conclusion: Ephedrine hydrochloride 30 mg IM 5 min before spinal anesthesia can be recommended for reduction of spinal anesthesia-induced hypotension in elective LSCS.

Key words: Apgar score, Ephedrine hydrochloride, Hypotension, Lower segment cesarean section, Mephentermine sulfate

INTRODUCTION

Spinal anesthesia causes blockade of sympathetic vasoconstrictor fibers resulting in venous dilation and pooling of blood in lower extremity causes hypotension which is more aggravated in pregnant patients due to aortocaval compression by the gravid uterus. Hypotension is especially deleterious in obstetrics patients where it affects both mother as well as fetus. Effects of hypotension on fetus are due to decrease uteroplacental blood flow causes fetal bradycardia, depression, and decreased Apgar score.¹⁻⁶

Numerous agents have been used in an effort to minimize the incidence of hypotension, i.e., fluid preloading either crystalloids or colloids, specific positioning, i.e., leg raising,
inflatable splints, using tourniquet, graded stockings up to mid-thigh, judicial use of Esmarch’s bandage, and judicious use of vasopressors such as methergine, parepdrine, metaraminol, dopamine, dobutamine, and mephentermine.7–11

Ephedrine has potent alpha and weak beta stimulatory effects. Due to its alpha receptor effect, it increases heart rate (HR) and cardiac output and has less effect on the peripheral vasculature. Ephedrine is most commonly used vasopressors to treat hypotension in obstetric patients.

Mephentermine increases blood pressure and cardiac output by catecholamine secretion which causes profound vasoconstriction and decreases uteroplacental blood flow.

Considering these facts present study was carried to evaluate and compare the effects of intramuscular (IM) ephedrine hydrochloride and mephentermine sulfate for reduction of spinal anesthesia-induced hypotension in lower segment cesarean section (LSCS), to compare the neonatal Apgar score and to compare other side effects.12–16

**MATERIALS AND METHODS**

The present study was carried out at the S.S. Medical College and associated Sanjay Gandhi Memorial Hospital, Rewa, Madhya Pradesh, from August 2014 to July 2015.

After approval from the Institutional Ethical Committee, the study was carried out on 90 healthy full-term pregnant female patients of age 20–35 years of American Society of Anesthesiologists Grade I and II, posted for elective LSCS under spinal anesthesia.

Patients, with known hypersensitivity to injection bupivacaine, having antepartum hemorrhage, pregnancy-induced hypertension, twin pregnancy, placenta previa, cord prolapsed, cardiac disease (ischemic heart diseases, valvular heart diseases, left ventricular failure, atrioventricular conduction block, and uncontrolled hypertension), renal dysfunction, deranged liver function test, and endocrinal or neurological disorders were excluded from the study. Procedure was explained and written informed consent was obtained from the patients.

Around 90 patients who fulfill all selection criteria were randomly divided into three groups of 30 patients each.

1. Group I - receiving 1 ml injection normal saline intramuscularly 5 min before giving spinal anesthesia
2. Group II - receiving 30 mg injection mephentermine sulfate intramuscularly 5 min before giving spinal anesthesia
3. Group III - receiving 30 mg injection ephedrine hydrochloride intramuscularly 5 min before giving spinal anesthesia.

All patients were kept nil orally for at least 6 h before surgery. After shifting the patients to operating table, monitors for non-invasive blood pressure, electrocardiogram, and pulse oximeter were attached. Two intravenous (IV) lines were secured. All the patients were preloaded with 10 ml/kg body weight Ringer lactate solution. After preloading baseline parameters, HR, systolic blood pressure (SBP), diastolic blood pressure (DBP), and SPO2 were recorded.

All the patients were uniformly premeditated with injection glycopyrrolate 0.2 mg IV, injection ranitidine 50 mg IV, and injection ondansetron 4 mg IV. The study drug was provided as coded identical syringes, as per randomization protocol and was injected intramuscularly 5 min before giving spinal anesthesia.

Patients were reassured and explained about the procedure and lumbar puncture was performed in L4-L5 interspace with 25-gauge standard wire gauge needle in left lateral position after confirming free flow of cerebrospinal fluid subarachnoid block (SAB) was given with injection 0.5% heavy bupivacaine 2.2 ml; then, patients were made supine, wedge was applied under right buttock, and observation was made for HR, SBP, DBP, and SPO2 at every 2 min interval for first 20 min and then every 5 min up to 1 h.

After confirmation of sensory block by pinprick method with 26-gauge needle up to T5-T6 level, surgery was started. After cord clamp of fetus injection oxytocin 10 IU IV was given in infusion and injection ergometrine 0.25 mg IV was given. Apgar score was also noted at 1 min and 5 min after delivery.

SBP <90 mm Hg or more than 20% fall below baseline was considered as hypotension and was treated by IV fluids and injection ephedrine 6 mg IV.

HR <60 bpm or more than 20% decrease from baseline was considered bradycardia and treated with injection atropine 0.6 mg intravenously.

Simultaneously, any other side effects such as nausea, vomiting, pain, discomfort, and chills and rigors were noted and managed accordingly.

At the end of the study, the observations were decoded, tabulated, and statistically analyzed using mean, standard deviation, P value, and Student’s t-test. For comparison, P < 0.05 was taken to be statistically significant and <0.0001 was taken to be highly significant.
RESULTS AND DISCUSSION

Spinal anesthesia is a popular technique for LSCS. It has several advantages over general anesthesia such as less stress, effective motor and sensory block, fewer chances of aspiration pneumonitis, difficult or failed intubation. Apart from these advantages, it has got some complications. Out of them, hypotension is the most common and immediate complication. This is due to the sympathetic blockade which causes decreased arteriolar and venous tone and decreased venous return. Vasopressors are the mainstay for prevention and treatment of hypotension following spinal anesthesia. Ephedrine is the most commonly recommended vasopressor to treat hypotension in obstetric patients. Vasopressors can be given by IM or IV routes.

In our study, all the patients in all the three groups were comparable to each other with respect to age, weight, height, time interval SAB-delivery, and duration of surgery as shown in Table 1.

Baseline SBP was 116.9 ± 7.99, 118 ± 7.91, and 120.6 ± 8.29 in Groups I, II, and III, respectively, which was comparable in all groups. After injecting the study drug, there was increase in SBP in Groups II and III, but there was no increase SBP in patients of Group I. Maximum fall in SBP was recorded from 2 to 10 min after giving spinal anesthesia, and it was 98.0 ± 7.1, 109.5 ± 12.32, and 107.6 ± 6.33 in Groups I, II, and III, respectively. Fall in SBP was significantly lower and earlier in Group I (2-5 min after spinal) as compared to Groups II and III (3-8 min after spinal). Fall in SBP was comparable in Groups II and III. At the end of surgery, SBP was comparable in all groups. This delay of fall in blood pressure and less number of patients in Groups II and III is due to drug-induced stimulation of alpha and beta receptors and increase in cardiac output which overcomes the effects of spinal anesthesia. Recovery in SBP starts after 10-20 min due to delivery of fetus and vasoconstrictor effect of ergometrine (Table 2).

Baseline DBP was 74 ± 7.3, 76 ± 8.5, and 77.47 ± 5.9 in Groups I, II, and III, respectively, which is comparable in all groups. After injecting the study drug, increase in DBP in Groups II and III was not significant. After SAB, there was a significant decrease in DBP in Group I as compared to Groups II and III. It was 60.4 ± 10.5, 69.4 ± 12.4, and 68.4 ± 8.8 in Groups I, II, and III, respectively. At the end of surgery, DBP was comparable in all groups (Table 3).

In our study, incidence of hypotension was 60% (18 patients), 23.33% (7 patients), and 26.66% (8 patients) in Groups I, II, and III, respectively. There was significantly higher incidence of hypotension in Group I as compared to Groups II and III. This can adversely affect mother as well fetus. Hypotension was treated with IV ephedrine. Rescue dose of ephedrine requirement was 6 mg in 15 patients in Group I as compared to 7 patients in Group II and 8 patients in Group III. Dose of ephedrine 9 mg was required in 3 patients in Group I, and in Groups II and III, any patient did not require this dose so less amount of rescue drug is require in Groups II and III (Table 4).

Similar results were found in a study of Grubb et al. 2004. They studied IM ephedrine 50 mg for reduction of spinal anesthesia-induced hypotension in LSCS and observed hypotension in 70% patients in the control group and 25% in ephedrine group.

Loughrey et al., 2002 studied ephedrine in dose of 6 mg and 12 mg IV with control and observed hypotension in 27% in E 12 group as compared to 60% in control group.

Cucchiara and Restall, 1973 studied the effects of IM mephenetermine 30 mg after spinal anesthesia in elderly

Table 1: Patients characteristics

<table>
<thead>
<tr>
<th>Patients characteristics</th>
<th>Group I</th>
<th>Group II</th>
<th>Group III</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>24.7±4.75</td>
<td>25±4.57</td>
<td>24.3±4.36</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Weight (kgs)</td>
<td>54.5±6.1</td>
<td>53.8±6.2</td>
<td>53.3±5.3</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>153±6.47</td>
<td>154±6.3</td>
<td>153±6.3</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Duration of Surgery (min)</td>
<td>42.1±5.58</td>
<td>42.33±4.31</td>
<td>43.0±5.51</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Time interval SAB-delivery</td>
<td>8.53±1.13</td>
<td>7.73±0.69</td>
<td>8.63±1.03</td>
<td>&gt;0.05</td>
</tr>
</tbody>
</table>

SAB: Subarachnoid block

Table 2: SBP

<table>
<thead>
<tr>
<th>Time interval of SBP</th>
<th>Group I</th>
<th>Group II</th>
<th>Group III</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>116.9±7.99</td>
<td>118±7.91</td>
<td>120.6±8.29</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>0 min</td>
<td>117.9±7.37</td>
<td>121±7.3</td>
<td>122.2±7.35</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>5 min</td>
<td>98.7±10.47</td>
<td>109.5±12.32</td>
<td>108.7±6.09</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>10 min</td>
<td>98.0±7.1</td>
<td>109.8±5.36</td>
<td>107.6±6.33</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>20 min</td>
<td>109.4±4.84</td>
<td>113.7±10.26</td>
<td>115.9±9.4</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>30 min</td>
<td>109.1±9.4</td>
<td>118.8±9.5</td>
<td>115.0±7.09</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>End of surgery</td>
<td>112±13.2</td>
<td>114±10</td>
<td>111.6±9.07</td>
<td>&gt;0.05</td>
</tr>
</tbody>
</table>

SBP: Systolic blood pressure

patients undergoing transurethral resection of prostate and observed hypotension in 24% patients of mephentermine group.

Vercauteren et al., 2000 studied the effects of IV ephedrine 5 mg after low-dose spinal anesthesia and observed hypotension in 25% patients of ephedrine group as compared to 55% patients in control group.

Similar results were not found in studies of Ayorinde et al., 2001. They compare the ephedrine 45 mg IM after spinal anesthesia in LSCS with phenylephrine 4 mg and control group and observed hypotension in 70% patients in control compared to 45% patients in ephedrine group.

Webb and Shipton, 1998 observed the incidence of hypotension after spinal anesthesia in 50% of patients of 37.5 mg ephedrine IM as compared to 80% of patients in control group.

Baseline HR was comparable in all groups. After injecting the drug, HR was comparable in all groups. After SAB, there was an increase in HR in all groups but, in Group I, it was significantly higher as compared to Groups II and III (Table 5). As HR was increased when blood pressure tends to fall. Similar results were found Ayorinde et al., 2001, Sahu et al., 2003, and Nagan Kee et al., 2001 observed a similar increase in HR.

Hypotension causes reduction in uteroplacental blood flow. Even short duration of hypotension causes fetal hypoxia and bradycardia. Apgar score was > or = to 7 in all patients at 1 min and 5 min, but on statistical analysis, it was significantly lower in Group II as compared to Groups I and III (Table 6). The incidence of low Apgar score in Group II was not found in literature but may be due to decrease uteroplacental blood flow. Ayorinde et al., 2001 observed similar results with ephedrine. They did not

**Table 4: Incidence of hypotension**

<table>
<thead>
<tr>
<th>Hypotension</th>
<th>Group I</th>
<th>Group II</th>
<th>Group III</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>18</td>
<td>7</td>
<td>8</td>
</tr>
</tbody>
</table>

**Table 5 HR**

<table>
<thead>
<tr>
<th>Time interval of HR</th>
<th>Group I</th>
<th>Group II</th>
<th>Group III</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Group I versus Group II</td>
<td>Group I versus Group III</td>
<td>Group II versus Group III</td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>102.5±10.2</td>
<td>87.4±12.38</td>
<td>85.93±11.14</td>
<td>0.936</td>
</tr>
<tr>
<td>0 min</td>
<td>103.9±8.6</td>
<td>86±10.85</td>
<td>84.87±9.63</td>
<td>0.108</td>
</tr>
<tr>
<td>5 min</td>
<td>116±25.68</td>
<td>85.53±10.01</td>
<td>83±9.6</td>
<td>0.022</td>
</tr>
<tr>
<td>10 min</td>
<td>116.25±8.3</td>
<td>84.58±8.62</td>
<td>82.43±8.84</td>
<td>0.0016</td>
</tr>
<tr>
<td>20 min</td>
<td>91.4±4.93</td>
<td>83.23±8.87</td>
<td>82.2±9.28</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>30 min</td>
<td>93.7±4.10</td>
<td>83.2±9.42</td>
<td>81.87±9.55</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>End of surgery</td>
<td>94.9±7.64</td>
<td>82.5±9.27</td>
<td>81±10.41</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

HR: Heart rate

**Table 6: Apgar score at 1 min and 5 min**

<table>
<thead>
<tr>
<th>Apgar score</th>
<th>Group I</th>
<th>Group II</th>
<th>Group III</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Group I versus Group II</td>
<td>Group II versus Group III</td>
<td>Group I versus Group III</td>
<td></td>
</tr>
<tr>
<td>At 1 min</td>
<td>8.5±0.53</td>
<td>7.7±0.69</td>
<td>8.7±0.47</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>At 5 min</td>
<td>9.5±0.5</td>
<td>9.26±0.69</td>
<td>9.7±0.5</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>
find any difference in Apgar score as compared to control group. Sahu et al., 2003\textsuperscript{13} observed Apgar score >7 or = in all patients of ephedrine, mephentermine, and control groups. Apgar score is better in patients operated under regional anesthesia than general anesthesia. It was observed by Marx et al., 1969\textsuperscript{10} and James et al., 1977.\textsuperscript{7} They observed Apgar score at 1 min was lowest with general anesthesia.

Brady cardia was not found in any of the patients in our study may be due to the level of spinal is T5-T6 and inotropic effect of ephedrine hydrochloride or injection mephentermine sulfate (Table 7).

Complained of nausea and vomiting were seen in 12 patients of Group I as compared to 5 patients in Group II and 5 patients in Group III. Higher incidence of nausea and vomiting in Group I patients is due to higher incidence of hypotension (Table 7).

Pain (retrosternal) was found in 9 patients of group and 10 patients each in Groups II and III (Table 7).

Chills and rigors were found in 2 patients each in Groups I and II and 3 patients in Group III. This was comparable in all groups (Table 7).

All complications are managed accordingly.

**CONCLUSION**

From the present study, the following conclusions can be drawn:

- Mephentermine sulfate is equally efficacious than ephedrine hydrochloride for prevention of spinal anesthesia-induced hypotension in pregnant patients undergoing LSCS
- Apgar score was lower in patients receiving mephentermine sulfate as compared to ephedrine hydrochloride, but it was never below 7 in all patients of all groups
- Neonatal outcome was good in all patients of all groups
- Both mephentermine sulfate and ephedrine hydrochloride have similar side effects.

**REFERENCES**

Evaluation of Breast Diseases on Patients Attending Rajiv Gandhi Institute of Medical Sciences General Hospital, Srikakulam

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²Assistant Professor, Department of General Surgery, Rajiv Gandhi Institute of Medical Sciences, Srikakulam, Andhra Pradesh, India,
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Abstract

Background: Patients often attend the surgical outpatient department (OPD) with the complaint of a lump with apprehension of malignancy. Early diagnosis allays the fear, and early recognition of malignancy saves the patient from metastatic breast disease.

Materials and Methods: A total of 348 patients were included in the present study. The data of the patients who presented with a breast lump and attended the surgical OPD of RIMS general hospital in Srikakulam. Patient’s age, sex, duration of the swelling, parity, symptoms such as pain, discharge from the nipple, size of the swelling, previous breast disease, side and quadrant of the breast involved, clinical diagnosis, histological diagnosis made by fine-needle aspiration cytology, and biopsy were recorded. All the results were analyzed.

Results: Out of the 348 patients included in the study, 18 patients were males and 330 patients were females. Among the females, 9 patients were prepubertal and 220 patients were pre-menopausal and rest of the 119 patients were post-menopausal. 94 patients were nulliparous. The lump was painless in 174 patients.

Conclusion: According to our study, the breast lump was the most common complaint. Most patients presenting late of more than 1 year. Fibroadenoma is more common than malignancy. Our results are consistent with literature and with other studies conducted elsewhere.

Key words: Biopsy, Benign, FNAC, Fibrosdenoma, Malignant

INTRODUCTION

Carcinoma of breast is the most common malignancy in the world with an incidence of 15.4%. Lump in the breast is the most common complaint of the female patients attending the surgical outpatient department (OPD). Various types of lesions ranging from inflammation to malignancy can occur in breast some can occur in the younger age group, whereas others in elderly age group. Early presentation and prompt evaluation are essential. In case of carcinoma, it can save the patient from developing metastasis and improve the prognosis.

MATERIALS AND METHODS

Our study is aimed at evaluating the incidence of breast disorders of the patients attending the surgical OPD of RIMS general Hospital Srikakulam and to compare with the findings available in literature. The study is done retrospectively from available data such as age, sex, presenting complaint, duration of complaint, and associated symptoms family.

A total of 348 patients were included in this study who attended with complaints of breast disorders to the surgical OPD of RIMS General Hospital from 1st August 2013 to 30th July 2016.
Inclusion Criteria
1. Symptomatic or asymptomatic patients complaining of lump in the breast with or without nodularity in the breast.
2. Presence of lump in the breast and nipple discharge.
3. Non-lactating breast abscess.

Exclusion Criteria
1. Acute lactating breast abscess
2. Male patients with lump in breast.

All the results were analyzed by Statistical Package for Social Sciences software. Chi-square test was used to measure the level of significance.

RESULTS
Out of the 348 patients included in the study, 18 patients were males and 330 patients were females. Among the females 9 patients were pre-pubertal and 220 patients were pre-menopausal and rest of the 119 patients were post-menopausal. The lump was painless in 174 patients. The most common age group involved in 25 to 40 years (Table 2). Fibro adenoma is the most common breast swelling (36.72%). Incidence of breast carcinoma was 27.87%. Left breast is most commonly involved.

Duration of Lump from Discovery to Presentation
- <1 month: 38
- 1 month to 3 months: 47
- 3 months to 6 months: 51
- 6 months to 12 months: 42
- More than 1 year: 160
- Lt breast is most affected: 157 (45.11%)
- Rt breast is affected: 121 (34.77%)
- Bilateral involvement: 60 (17.24%).

The most common age group involved is 25-40 years (136 cases 40%) (Tables 1 and 3). Biopsy in the form of fine-needle aspiration cytology, core needle biopsy, and excision biopsy was done in 285 cases. 78 patients do not require biopsy, and 12 patients refused. 128 patients (36.72%) were found to be having fibroadenoma. 97 patients (27.87%) were found to be having invasive carcinoma (Ductal cell carcinoma). The mean age for breast cancer is 46.3 years, range 35-70 years with a peak of 55 years. For fibroadenoma, mean age was 24.2 years; median 23 years range 15-46 years with a peak age of 23.

DISCUSSION
A breast lump is the most common complaint of breast disease both in males and females. Although most breast lumps are benign, the true nature of the lump cannot be made by clinical examination only. A definite diagnosis can

<table>
<thead>
<tr>
<th>Table 1: Age distribution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age in years</td>
</tr>
<tr>
<td>&lt;20</td>
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<tr>
<td>21-30</td>
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<td>31-40</td>
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<tr>
<td>41-60</td>
</tr>
<tr>
<td>51-60</td>
</tr>
<tr>
<td>61-70</td>
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<table>
<thead>
<tr>
<th>Table 2: Sex distribution</th>
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</thead>
<tbody>
<tr>
<td>Sex</td>
</tr>
<tr>
<td>Males</td>
</tr>
<tr>
<td>Females</td>
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<table>
<thead>
<tr>
<th>Table 3: Quadrant-wise distribution</th>
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</thead>
<tbody>
<tr>
<td>Quadrant</td>
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<tr>
<td>----------------</td>
</tr>
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<td></td>
</tr>
<tr>
<td>Lower</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Central</td>
</tr>
<tr>
<td>Whole</td>
</tr>
<tr>
<td>Multiple</td>
</tr>
</tbody>
</table>
be made by histopathology. Many patients of carcinoma breast of Srikakulam as with other parts of India present late with ulceration, fungation, axillary lymphadenopathy, and liver secondaries due to ignorance and poverty. Early diagnosis and treatment saves the patient from mortality and morbidity and saves the patient from expensive treatment of advanced disease. 1-3 Fortunately, studies have shown that the majority of patients presenting to the department have benign disease. Most of these patients still present late to the hospital with 45.97% of patients presenting more than 1 year of duration of their disease. In a similar study by Goyal et al., 4 40.86% of patients presented with more than 1 year of duration of their disease. Okobia and Aligbe 5 noted that in their study 78% of their patients presented after 3 months of noticing the lump. In a study, 4 82.6% patients presented after a month of noticing the lump. Fibroadenoma is the most common clinical diagnosis (36.77%) followed by carcinoma of breast (27.8%) in our study (Table 4). After histopathological examination, fibroadenoma is the most common (39.9%) followed by carcinoma of breast (23.85%) (Table 5). In a study by Choudhary, fibroadenoma is common (46.2%) followed by carcinoma (35.9%). 6–10 66.15% of diseases are benign in our study, whereas it is 64%, 4 2.6% (Eku), and 90% (Zakaria). Studies by Mayun, Khan, Pradhan, Siddique Hadshon, fibroadenoma to be the most common cause of breast lump and fibrocystic disease than breast cancer, the age range of breast lump in our study is 12 to 74 years with most patients are in the age group of 25-35 years. Carcinoma of breast is most commonly seen in the age group of 40-50 years consistent with literature. In our study, fibroadenoma is most commonly seen in the age group of 20-40 years age group with median of 24.1 years. This once again emphasizes that any breast swelling in the females of the age group of 35-50 year to be considered as carcinoma of breast until proved otherwise. 6–10

In our study, we found 8 cases of gynecomastia, 11 cases of phyllodes tumors, 2 cases of antioboma, and 1 case of tuberculous mastitis. Retrospective study on the demographic pattern on breast lumps operated at the University of Maiduguri Teaching Hospital over a period of 6-year by Nuhu et al. concluded though benign breast diseases still common, a high percentage of cases in Maiduguri are due to malignancy, and this is found be increasing in younger age group. Prajapati et al. retrospectively analyzed the clinicopathological review of the breast diseases on 550 patients attended to the surgical OPD of a teaching hospital with a complaint of breast diseases from January 2008 to December 2012. They concluded that breast lump is the most common complaint and most patients presenting late. 11,12

CONCLUSION

According to our study, the breast lump was the most common complaint most patients presenting late more than 1 year. Fibroadenoma is more common than malignancy.

Table 4: Clinical diagnosis of patients

<table>
<thead>
<tr>
<th>Clinical diagnosis</th>
<th>Number of patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carcinoma of breast</td>
<td>97 (27.87)</td>
</tr>
<tr>
<td>Fibroadenoma</td>
<td>128 (36.78)</td>
</tr>
<tr>
<td>Duct ectasia</td>
<td>24 (6.89)</td>
</tr>
<tr>
<td>Mastitis</td>
<td>28 (8.04)</td>
</tr>
<tr>
<td>Fibrocystic diseases</td>
<td>21 (6.03)</td>
</tr>
<tr>
<td>Abscess</td>
<td>28 (8.04)</td>
</tr>
<tr>
<td>Galactocele</td>
<td>11 (3.16)</td>
</tr>
<tr>
<td>Phyllodes tumor</td>
<td>8 (2.29)</td>
</tr>
<tr>
<td>None</td>
<td>3 (0.86)</td>
</tr>
</tbody>
</table>

Table 5: Histopathology

<table>
<thead>
<tr>
<th>Histopathological diagnosis</th>
<th>Number of patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fibroadenoma</td>
<td>139 (40)</td>
</tr>
<tr>
<td>Carcinoma of breast and ductal cell lobular</td>
<td>83 (23.82)</td>
</tr>
<tr>
<td>Gynecomastia</td>
<td>8 (2.28)</td>
</tr>
<tr>
<td>Inflammatory</td>
<td>8 (2.28)</td>
</tr>
<tr>
<td>Breast disorders</td>
<td>13 (3.73)</td>
</tr>
<tr>
<td>Benign phyllodes tumor</td>
<td>11 (3.10)</td>
</tr>
<tr>
<td>Antiboma</td>
<td>2 (0.50)</td>
</tr>
<tr>
<td>Fibrocystic disease</td>
<td>32 (9.15)</td>
</tr>
<tr>
<td>Tuberculosis</td>
<td>1 (0.50)</td>
</tr>
<tr>
<td>Normal</td>
<td>8 (2.28)</td>
</tr>
</tbody>
</table>
Our results are consistent with literature and with other studies conducted elsewhere.

**REFERENCES**


**Source of Support:** Nil, **Conflict of Interest:** None declared.
Cervical Lymphadenopathy: A Prospective Study in Rajiv Gandhi Institute of Medical Sciences, Srikakulam, Andhra Pradesh

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Abstract

Background: Enlargement of cervical lymph nodes is the most common form of peripheral lymphadenopathy often encountered clinical entity in the surgical operative. Clinical evaluation and diagnosis is supported by fine-needle aspiration cytology (FNAC) or by biopsy.

Purpose: This study was done to evaluate the causes of cervical adenopathy in the patients attending Rajiv Gandhi Institute of Medical Sciences (RIMS) General Hospital, Srikakulam, Andhra Pradesh. Cytological findings of FNAC were compared with histological reports of biopsy.

Materials and Methods: This study was conducted on 146 patients who presented with a complaint of cervical lymphadenopathy to RIMS General Hospital, Srikakulam, from January 2015 to July 2016. A detailed history regarding duration, associated clinical features, family history were recorded. The complete clinical examination was done along with routine laboratory investigations including chest X-ray, and special tests, like Mantoux, was done for appropriate patients.

Results: A total of 146 patients were evaluated in our study. The various causes of cervical adenopathy according to cytomorphological patterns and their frequency of occurrence in relation to the age and sex groups and the cytology of FNAC were correlated with histopathology reports of the open biopsy of the excised lymph node. For FNAC, diagnostic accuracy of 93% was observed. The sensitivity and specificity of FNAC for various lesions was calculated in tables given in the article.

Conclusion: Tuberculosis is the most common cause of cervical lymphadenopathy and more than one-third (37.33%) of cases are seen in pediatric age group. FNAC is simple minimally invasive with least complications and with a diagnostic sensitivity of 93% and can be used as a primary investigatory tool.

Key words: Cervical lymphadenopathy, Fine-needle aspiration cytology, Histopathological examination, Tuberculosis

INTRODUCTION

Cervical lymphadenopathy implies an abnormal increase in size and altered consistency of lymph nodes. It is often used synonymously as swollen/enlarged lymph nodes. Cervical adenopathy is fairly common clinical presentation often poses a challenge to the attending clinician in making the diagnosis and in ascertaining the management of the disease. Cervical lymphadenopathy can present as an isolated feature or as part of generalized lymphadenopathy.¹² Cervical adenopathy is divided into: (1) Acute lymphadenopathy (less than 2 weeks duration), (2) subacute lymphadenopathy (2-6 weeks duration), and (3) chronic lymphadenopathy (more than 6 weeks duration).³ In pediatric age group, tuberculosis (TB) is the most common cause followed by pyogenic infections whereas in adults and older people carcinoma of head and neck region are the most common cause. These cases of cervical lymphadenopathy were evaluated clinically. Radiologically, pathologically by fine-needle aspiration cytology (FNAC) and biopsy of excised lymph nodes. As compared to open biopsy, FNAC has come up in a long
way as parallel but as a separate mode of investigation in the diagnosis of cervical lymphadenopathy. Diagnosis is obtained quickly. Complications are almost negligible and diagnostic accuracy is high.4

This study was done with the objective of evaluating the causes of cervical adenopathy and to find out the epidemiological factors pertaining to cervical lymphadenopathy and the role of FNAC as compared with an open biopsy.

MATERIALS AND METHODS

This study was done over the patients attending to the outpatient Department of Surgery of General Hospital of Rajiv Gandhi Institute of Medical Sciences, Srikakulam of Andhra Pradesh from January 2014 to July 2016 with a complaint of enlarged or swollen lymph nodes of the neck. A detailed history was taken and a note was made regarding age, sex, duration of symptoms and history of contact with a known TB patient. A complete physical examination of the patient is done with special reference to the size, number, site of the involvement, side, mobility, and consistency. Routine laboratory investigations such as total count, differential count, and erythrocyte sedimentation rate (ESR) were done and chest X-ray taken on suspected case of TB lymphadenitis. Special investigations like sputum for AFB, Mantoux test were done in suspected TB patients FNAC, and biopsy was done on the enlarged lymph nodes. The pathologist who performed the histopathological examination of biopsy specimen was unaware of FNAC findings. Finally, the results of FNAC and histopathological examination were compared for sensitivity, specificity - and diagnostic accuracy of FNAC was calculated.

OBSERVATIONS

A total of 146 patients were evaluated in our study. The various causes of cervical adenopathy according to cytomorphological patterns, and their frequency of occurrence in relation to the age and sex groups is shown in Table 1. Males were more commonly involved.

ESR was found to be raised in 53.42% of the cases. In the cases of TB lymphadenitis a history of contact is present in 19 cases. ESR was raised in 58 cases (77.33%). Co-existing active lesions of TB in X-ray chest are seen 7 cases (9.33%). Mantoux test was positive in 49 cases (65.33%). Hodgkin’s lymphoma - 11 cases. Non-Hodgkin’s lymphoma - 7 cases. Ratio of Hodgkin to non-Hodgkin is 1.58:1. Metastatic cervical nodes 18 cases primary was found in 11 cases. In metastatic lymph nodes, the most common histopathology is squamous cell carcinoma. The most common primary site found is an oral cavity (Palate – 2). Tongue 2 buccal mucosa (floor of the mouth). Next most primary site is thyroid. The most common histopathology of cervical metastases is squamous epithelium. The cytology of FNAC was correlated with histopathology reports of the open biopsy of the excised lymph node (Table 6). For FNAC, diagnostic accuracy of 93% was observed. The sensitivity and specificity of FNAC for various lessons was calculated in Table 7.

DISCUSSION

Lymph nodes are considered as fortress of immune defense.1

Lymph nodes are encapsulated centers of antigen presentation and lymphocytic activation, differentiation and proliferation. They produce mature, antigen-primed, B and T cells and filter particles, including microbes, from the lymph by the action of numerous phagocytocytic macrophages. These specialized immune cells named as lymphocytes, detect and combat the pathogens in the body. When inflamed these nodes get swollen, enlarges to produce the more number of lymphocytes.3

Howard and Lund had focused on an idea of having approximately 800 lymph nodes in our body and 300 of them are located in the cervical region alone.6 Cervical

<table>
<thead>
<tr>
<th>Table 1: Age distribution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lymphoma</td>
</tr>
<tr>
<td>M</td>
</tr>
<tr>
<td>---</td>
</tr>
<tr>
<td>0-10</td>
</tr>
<tr>
<td>11-20</td>
</tr>
<tr>
<td>21-30</td>
</tr>
<tr>
<td>31-40</td>
</tr>
<tr>
<td>41-50</td>
</tr>
<tr>
<td>51-60</td>
</tr>
<tr>
<td>61-70</td>
</tr>
<tr>
<td>71-80</td>
</tr>
<tr>
<td>Total</td>
</tr>
<tr>
<td></td>
</tr>
</tbody>
</table>
Lymphadenopathy has been defined as cervical lymph nodes measuring more than 1 cm in diameter. It is most frequent among all age groups. Significant anxiety surrounds the finding of cervical lymphadenopathy both to the patient and to the attending clinician, due to the concern of the underlying pathology. Numerous studies have been conducted on cervical lymphadenopathy. Cervical lymph nodes are the most frequently enlarged and biopsied nodes, of all the peripheral lymph nodes.

The most cases can be diagnosed on the basis of a careful history and detailed clinical examination. The causes include microbiological, hematological, neoplastic and connective tissue disorders. In our study, cervical lymphadenopathy is of non-neoplastic in 76% of cases, the incidence of neoplasia is 24%. These findings were consistent with the findings of Biswas et al. (2013). They found an incidence of non-neoplastic in 71.6% and neoplastic in 28.3% of the cases. In a similar study by Rajesh Kumar Padhy et al. (2015) found an incidence of non-neoplasia in 71% of the cases and neoplasia in 29%.

In our study, males are a more affected than females. Males to female ratio is 1.8:1. This is similar to the findings of the study by Rajesh Kumar Padhy et al. (2013), Pandav et al. (2012), Adhikari et al. (2011), who found male preponderance with a male to female ratio being 1.17:1, 1.07:1, 1.2:1, respectively. Cervical lymphadenopathy is most commonly seen in our study in the age group of 20-30 years (21.67%) followed by the age group of 30-40 years (16.5%), similar to studies by Rajesh Kumar et al. (22% in the age group of 20-30 years and 18% in the 4th decade). In another study, Dukare et al. (2014) reported an increased incidence of 23.34% in the 3rd decade and 15.49% in the 4th decade. Pandav et al. reported a maximum incidence in the 3rd decade 21%.9-15

Our findings are consistent with these findings. In this study, TB was the most common cause of lymphadenopathy (51.6%), followed by reactive/nonspecific lymphadenopathy (24.6%), consistent with findings of Rajesh Kumar et al. (TB 45%, reactive/non-specific 26%). Similarly, Vedi et al. (2013) reported TB in 50% of cases and in 30% of cases. Similar results have been highlighted in other studies. Lymphadenopathy is most commonly unilateral 76% and bilateral in 24% of our cases, right side is most frequently involved (43%). Our findings are consistent with other studies.16-20

### Table 2: Examination findings

<table>
<thead>
<tr>
<th>Variable</th>
<th>Tuberculous</th>
<th>Reactive</th>
<th>Hodgkin’s lymphoma</th>
<th>Non-Hodgkin’s lymphoma</th>
<th>Metastatic</th>
<th>Total (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Size (cm)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;3</td>
<td>48</td>
<td>28</td>
<td>2</td>
<td>2</td>
<td>4</td>
<td>85 (58.21)</td>
</tr>
<tr>
<td>3-6</td>
<td>23</td>
<td>8</td>
<td>8</td>
<td>8</td>
<td>6</td>
<td>49 (33.56)</td>
</tr>
<tr>
<td>&gt;6</td>
<td>4</td>
<td>0</td>
<td>0</td>
<td></td>
<td>8</td>
<td>8 (8.21)</td>
</tr>
<tr>
<td>Side</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unilateral</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right</td>
<td>41</td>
<td>19</td>
<td>3</td>
<td>1</td>
<td>9</td>
<td>73 (50)</td>
</tr>
<tr>
<td>Left</td>
<td>28</td>
<td>10</td>
<td>3</td>
<td>2</td>
<td>5</td>
<td>48 (32.87)</td>
</tr>
<tr>
<td>Bilateral</td>
<td>6</td>
<td>7</td>
<td>1</td>
<td>7</td>
<td>4</td>
<td>25 (17)</td>
</tr>
<tr>
<td>Consistency</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Soft</td>
<td>30</td>
<td>11</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>44 (30)</td>
</tr>
<tr>
<td>Firm</td>
<td>42</td>
<td>24</td>
<td>6</td>
<td>9</td>
<td>1</td>
<td>82 (56)</td>
</tr>
<tr>
<td>Hard</td>
<td>3</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>16</td>
<td>20 (14)</td>
</tr>
<tr>
<td>Mobile</td>
<td>71</td>
<td>34</td>
<td>6</td>
<td>9</td>
<td>6</td>
<td>106 (73)</td>
</tr>
<tr>
<td>Fixed</td>
<td>4</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>12</td>
<td>20 (14)</td>
</tr>
<tr>
<td>Number of groups</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Single</td>
<td>61</td>
<td>0</td>
<td>0</td>
<td>4</td>
<td>87</td>
<td>59 (58.58)</td>
</tr>
<tr>
<td>Two groups</td>
<td>8</td>
<td>3</td>
<td>6</td>
<td>8</td>
<td>34</td>
<td>23 (22.22)</td>
</tr>
<tr>
<td>&gt;2 groups</td>
<td>4</td>
<td>4</td>
<td>4</td>
<td>6</td>
<td>6</td>
<td>17 (17)</td>
</tr>
</tbody>
</table>

### Table 3: Site distribution of affected lymph nodes

<table>
<thead>
<tr>
<th>Site</th>
<th>Tuberculous lymphadenitis</th>
<th>Reactive</th>
<th>Hodgkin’s lymphoma</th>
<th>Non-Hodgkin’s lymphoma</th>
<th>Metastatic lymph adenitis</th>
<th>Total (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Level 1</td>
<td>3</td>
<td>9</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>15 (10)</td>
</tr>
<tr>
<td>Level 2</td>
<td>23</td>
<td>14</td>
<td>1</td>
<td>2</td>
<td>2</td>
<td>40 (27)</td>
</tr>
<tr>
<td>Level 3</td>
<td>7</td>
<td>1</td>
<td>6</td>
<td>1</td>
<td>3</td>
<td>14 (10)</td>
</tr>
<tr>
<td>Level 4</td>
<td>2</td>
<td>3</td>
<td>3</td>
<td>5</td>
<td>3</td>
<td>15 (10)</td>
</tr>
<tr>
<td>Level 5</td>
<td>40</td>
<td>13</td>
<td>6</td>
<td>9</td>
<td>4</td>
<td>72 (48)</td>
</tr>
<tr>
<td>Level 6</td>
<td>0</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>75</td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>
In this study (Table 2), 74.64% of lymph nodes are mobile while only 25.36% of lymph nodes are fixed to the surrounding structures. This finding is consistent with those of Rajesh et al. (mobile 80% fixed 20%), Chamyal and Sabarigrish (1997) found mobile lymphnodes in 60% and fixed nodes in 26%; of cases. In our study, a single group of lymphnodes found to be involved in 59.5% of cases and more than 2 groups involved in 17.21% of the cases. This study is in accordance with the study of Rajesh et al. who found results of 63% and 14%. Ismail and Mohammad (2013) found the figures of 60% for a single group and 12.7% for the involvement of more than 2 groups. The observed results are similar to the findings of Baskota et al. (2004) who found that a single group is involved in 68% of the cases and more than 2 groups were involved in 13% of the cases.20-25.

In this study (Tables 3 and 4), out of the 75 cases of TB lymphadenitis only 7 cases had coexisting active TB lesions confirmed by chest X-ray (9.33%). This finding is in accordance with findings of Daudopota et al. (2013) and Magsi et al. (2013) who had reported coexisting active TB lesions in chest in 3.64% and 7.5% cases, respectively. 19 cases had history of contact (24.66%) with a TB patient. This study is in accordance with that of Rajesh et al. and Ismail and Mohammad who reported a contact of 24.4% and 27%, respectively. Nodes were matted in 54 cases (72%) and discrete in 21 cases (28%).

In this study, out of 17 lymphoma cases, 11 cases are Hodgkin’s lymphoma and 6 cases are non-Hodgkin’s lymphoma. The ratio of Hodgkin’s to non-Hodgkin’s lymphoma is 1.5:1. The findings were similar to another study by Vedi et al. and by Rajesh et al. In this study (Table 5), metastases were present in 18 cases (12.33%). In 13 cases (72.23%), primary site of malignancy is found. In 28% cases the primary was not found. Out of the 13 cases in which the primary was found tumors of squamous

---

### Table 4: Tubercular lymphadenitis

<table>
<thead>
<tr>
<th>Chest X-ray</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive</td>
<td>7 (9.33)</td>
</tr>
<tr>
<td>Negative</td>
<td>68 (90.66)</td>
</tr>
<tr>
<td>Nodal status</td>
<td></td>
</tr>
<tr>
<td>Discrete</td>
<td>32</td>
</tr>
<tr>
<td>Matted</td>
<td>43 (42.66)</td>
</tr>
<tr>
<td>ESR (mm) &lt;20</td>
<td>17 (23)</td>
</tr>
<tr>
<td>&gt;20</td>
<td>58 (77.33)</td>
</tr>
<tr>
<td>Mantoux Positive</td>
<td>49 (65.33)</td>
</tr>
<tr>
<td>Negative</td>
<td>26 (34.66)</td>
</tr>
<tr>
<td>History of contact</td>
<td>19 (25)</td>
</tr>
</tbody>
</table>

### Table 5: Distribution of primary site in cases of metastatic secondaries in neck

<table>
<thead>
<tr>
<th>Primary site</th>
<th>Origin Site</th>
<th>Number of cases</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Known</td>
<td>Squamous cell of origin</td>
<td>Oral cavity</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Tongue/Buccal mucosa</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Palate</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Nasopharynx</td>
<td>1</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>Larynx</td>
<td>1</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>Lung</td>
<td>1</td>
<td>6</td>
</tr>
<tr>
<td>Non squamous cell of origin</td>
<td>Thyroid</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>Parotid</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
<td></td>
<td>7</td>
<td></td>
</tr>
</tbody>
</table>

### Table 6: Correlation of histopathological (biopsy) diagnosis and cytological (FNAC) diagnosis

<table>
<thead>
<tr>
<th>Clinical diagnosis</th>
<th>Number of FNAC cases</th>
<th>Number of histopathological diagnoses</th>
<th>Accuracy (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tuberculous</td>
<td>71</td>
<td>Tuberculous  69 3 1 1 0 2</td>
<td>95.7</td>
</tr>
<tr>
<td>Reactive</td>
<td>36</td>
<td>Reactive  4 30 1 0 1 83.7</td>
<td></td>
</tr>
<tr>
<td>Hodgkin’s lymphoma</td>
<td>7</td>
<td>Hodgkin’s lymphoma  0 1 6 85.52</td>
<td></td>
</tr>
<tr>
<td>Non-Hodgkin’s</td>
<td>11</td>
<td>Non-Hodgkin’s lymphoma  0 10 0 100.00</td>
<td></td>
</tr>
<tr>
<td>Metastatic</td>
<td>21</td>
<td>Metastatic  2 0 0 3 85.05</td>
<td></td>
</tr>
</tbody>
</table>

FNAC: Fine-needle aspiration cytology
Cervical lymphadenopathy

In the present study Metastatic/Biswas of 92% 90.9%, 88.4%. FNAC. 26-32

most common cause of non-squamous secondaries are in the neck is a primary malignancy of oral cavity, the primary modality of investigation in evaluating the cause is cheap, least invasive with least complications and a primary modality of investigation in evaluating the cause of lymphadenopathy.

CONCLUSION

Although open biopsy is the gold standard for diagnosis of cervical lymphadenopathy, equal results were seen with FNAC. Open biopsy is associated with higher incidence of complications FNAC is least expensive, minimal invasive, associated with minimal complications (Table 8).

REFERENCES


| Table 7: Sensitivity and Specificity of FNAC in Cervical lymphadenopathy |
|-----------------------------|-----------------------------|
| FNAC diagnosis              | Sensitivity (%) | Specificity (%) |
| Tuberculosis                | 95.7            | 96.86           |
| Reactive/non-specific       | 83.7            | 95.66           |
| Lymphoma                    | 85.52           | 100             |
| Metastatic secondaries      | 85.05           | 97.0            |

FNAC: Fine-needle aspiration cytology

origin were (61%). Non-squamous tumors origin was 39%. Among the non-squamous, the primary is found in thyroid (22.22%) and parotid (5.5%). In the squamous group, the primary is most commonly seen in oral cavity (60%) and nasopharynx (20%) and lung and larynx (20%). These results were similar to those of Prasad and Mohan (2014). They reported primary in the oral cavity in 48.5% of the cases. In another study by Afroz et al. in non-squamous metastatic deposits primary is found in thyroid in 15.09% of the cases.

The overall diagnostic accuracy of FNAC in the case of cervical lymphadenopathy in our study is 95%. Which is similar to the results of Rajesh et al. (2015), Adhikari et al. (2011) 11, and Biswas et al. who reported an overall accuracy of 92% 90.9%, 88.4%. FNAC. 26-32

| Table 8: Diagnostic Accuracy of FNAC |
|-----------------------------|-----------------------------|
| In present study            | Tuberculous lymphadenopathy | Sensitivity (95%) | Specificity (97%) |
| Study by Rajesh             | 91.11                       | 93.6             |
| Biswas S et al. (2014)      | 86.6                        | 100              |
| Shrestha et al. (2010)      | 85.71                       | 94.82            |
| In present study            | Non-specific/reactive       | 83.7            | 94.5             |
| Study by Rajesh             | 88.65                       | 95.96            |
| Quadri et al. (2012)        | 86                          | 95.9             |
| In present study            | Lymphoma                    | 85.7            | 100              |
| Rajesh                      | 75                          | 100              |
| Singh et al. (2014)         | 81.4                        | 99.3             |
| In the present study        | Metastatic/secondaries       | 85.5            | 97.25            |
| Rajesh et al.               | 83.6                        | 96.20            |
| Biswas et al. (27)          | 100                         | 96.15            |

Although open biopsy is the gold standard for diagnosis of cervical lymphadenopathy, equal results were seen with FNAC. Open biopsy is associated with higher incidence of complications FNAC is least expensive, minimal invasive, associated with minimal complications (Table 8).

TB Lymphadenitis is the most common cause of cervical lymphadenitis followed by reactive and metastatic secondaries. The most common cause of secondaries in the neck is a primary malignancy of oral cavity, the most common cause of non-squamous secondaries are secondary to malignancy of Thyroid. Although open biopsy of lymph nodes is the gold standard, FNAC is cheap, least invasive with least complications and a primary modality of investigation in evaluating the cause of lymphadenopathy.


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Anesthetic Considerations and Management of Obstetric Hemorrhage

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INTRODUCTION

A major obstetric hemorrhage remains one of the leading causes of maternal mortality and morbidity worldwide.1 A study by world health organization revealed that 25-30% of maternal deaths are due to peripartum hemorrhage globally.2 Despite the widespread reduction in maternal deaths due to improved antepartum, intrapartum and postpartum care in developed nations, mortality rates are persistently high in many countries which are unable to provide advanced medical care. Postpartum hemorrhage accounts for a substantial proportion of maternal deaths in developing countries.3 A lot of literature is available regarding causes, prevention, and management of massive obstetric hemorrhage (MOH). We have tried to compile the literature and include the latest developments in this field. This article aims to provide a practical and pragmatic approach to the management of MOH, coagulopathy associated with it, although it is recognized that due to limited evidence, expert opinion will vary.

Management of MOH is often challenging due to many contributing factors. Blood loss can be underestimated because bleeding may be concealed and the presence of amniotic fluid makes accurate measurement difficult. The physiological changes of pregnancy mask the magnitude of the blood loss.4 Serious morbidity resulting from hemorrhage includes adult respiratory distress syndrome, coagulopathy, shock, loss of fertility, and pituitary necrosis.5

METHODS

An extensive literature search was performed through Medline, PubMed, and Google scholar using the keywords
such as postpartum hemorrhage, thromboelastography (TEG), pregnancy, fibrinogen, and operative blood salvage. Abstracts from potentially relevant publications were also studied. In this narrative review, we have discussed the various causes of MOH, management of unanticipated hemorrhage, massive transfusion protocols, and anesthesia concerns, especially if emergency hysterectomy is to be done.

CAUSES OF OBSTETRIC HEMORRHAGE

Obstetric hemorrhage is classified into antepartum, intrapartum, and postpartum hemorrhage (Table 1).

Antepartum Hemorrhage

Antepartum hemorrhage is defined as bleeding from genital tract after 24 weeks of gestation and has an incidence of 2-5% of all pregnancies beyond 24 weeks. APH represents a greater threat to fetus than mother and fetal compromise may precede maternal complications. Placenta previa and abruption are major causes of significant hemorrhage in the third trimester.

Placenta previa

In placenta previa, there is an abnormal implantation of placenta in the lower uterine segment. Placenta accreta, increta, and percreta are conditions of abnormal placentation in which there is an increasing degree of abnormal invasion of the placenta into the myometrium. The presence of placenta previa increases the likelihood that the patient will require a peripartum hysterectomy. The classic sign of placenta previa is painless vaginal bleeding during the second or third trimester.

Cesarean section is the recommended mode of delivery. Patients with placenta previa are at significantly increased risk for high intraoperative blood loss due to the possibility of the obstetrician incising through the placenta and the increased risk for placenta accrete. The uterine site of abnormal implantation does not contract as efficiently as a normal uterine segment which leads to increased bleeding.

Table 1: Causes of obstetric hemorrhage

<table>
<thead>
<tr>
<th>Causes of hemorrhage</th>
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<tr>
<td>Antepartum hemorrhage</td>
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<td>Placenta previa</td>
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<td>Placental abruption</td>
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<tr>
<td>Genetic coagulopathies</td>
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<tr>
<td>Postpartum hemorrhage</td>
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<tr>
<td>Uterine atony</td>
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<tr>
<td>Placenta accreta/increta/percreta</td>
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<tr>
<td>Retained placenta</td>
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<td>Lacerations during vaginal delivery</td>
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Placental abruption

Hemorrhage arising from premature separation of a normally situated placenta is known as placental abruption. Risk factors include maternal hypertension, multiparity, uterine over distension, previous abruption, advanced maternal age, and abdominal trauma. There is often associated increased uterine tone, abdominal pain, and premature labor. Fetal distress is a common and can be the presenting feature.

In cases of concealed abruption, vaginal bleeding can be absent and an underestimation of maternal hypovolemia may occur. The major complications of abruption include hemorrhagic shock, acute renal failure, coagulopathy, and fetal demise. Abruption is the most common cause of disseminated intravascular coagulation in pregnancy.

Uterine rupture

Uterine rupture is the most life-threatening emergency in obstetrics associated with high maternal and perinatal morbidity and mortality. Risk factors include prior uterine surgery, trauma, uterine anomalies, dystocia, use of uterotonic drugs, and abnormal placentation. Clinical presentation can vary from subtle findings such as uterine tenderness and non-reassuring fetal heart rate patterns to severe localized abdominal pain and a rapid onset of maternal hypovolemic shock.

Fetal delivery with repair of ruptured uterine wall is the definitive treatment. Uterine and internal iliac arterial ligation may be done in anticipated cases. In intractable blood loss as a last resort, obstetric hysterectomy is advocated without wasting time in decision making.

Postpartum Hemorrhage

Postpartum hemorrhage is defined as blood loss of 500 ml or more from genital tract in the first 24 h of delivery. Massive PPH is defined as the blood loss of 1000 ml or more. It can be further subdivided into minor (500-1000 ml) or major (>1000 ml).

Blood loss is frequently underestimated and physiological variables especially that of systolic blood pressure (BP) may change little until 30-40% of circulating blood volume has been lost. High index of suspicion for major obstetric hemorrhage must be maintained.

MANAGEMENT OF MOH

MOH is defined as blood loss from the uterus or genital tract >1500 ml or decrease in hemoglobin of >4 g/dl or acute loss requiring transfusion of more than 4 units of blood.
Prevention
- Avoidance of prolonged labor.
- Minimal trauma during assisted vaginal delivery.
- Detection and treatment of anemia during pregnancy.
- Identification of placenta previa by antenatal ultrasound examination.
- Magnetic resonance imaging (MRI) to determine placenta accreta/percreta. If present then multidisciplinary planning is required.
- Active management of the third stage as below
  1. Early clamping of umbilical cord
  2. Controlled cord traction for placental delivery and prophylactic administration of uterotonics at delivery (e.g., oxytocin).
  3. A long acting oxytocin derivative carbetocin (single dose of 100 µg) is at least as effective as oxytocin.\textsuperscript{7,18}

Women experiencing obstetric hemorrhage are in good health, young and initially compensate well for losses due to the hypovolemia until the circulating blood volume is very low. Modified early obstetric warning system (MEOWS) is a useful bedside tool for predicting morbidity of these patients and is recommended in all obstetric patients. It is helpful to track maternal physiological parameters and to aid early recognition and treatment.\textsuperscript{1} Blood loss is generally underestimated both in volume and rapidity.\textsuperscript{19} Blood loss may be concealed and difficult to calculate. Thus, MEOWS includes looking for signs such as tachycardia, hypotension, decreased urine output, pallor, lower abdominal pain, and cold peripheries.\textsuperscript{1} The “rule of 30” is useful if the patients systolic BP drops by 30 %, the heart rate rises by 30 %, the respiratory rate increase to more than 30/min, the hemoglobin or hematocrit drops by 30 % and the urine output decreases to <30 ml/h, the patient is likely to have lost 30% of her blood volume. The “shock index” defined as the heart rate divided by systolic BP (normal up to 0.9 in obstetrics) has been shown to be an accurate indicator of compensatory changes in the chorionic villus sampling due to blood loss. Active periodic estimation improves the accuracy of estimation.\textsuperscript{20} According to one study, there was 16% underestimation at 300 ml blood loss which rose to 41% at 2000 ml loss.\textsuperscript{21}

Management depends on whether the MOH is anticipated/unanticipated.

Anticipated MOH
If anticipated as in patient of low lying placenta or uterine scar, placenta accreta, we should keep two large bore intravenous cannulae ready with rapid infusion device/pressure bags, cross-matched blood, and blood warmer. Invasive monitoring, cell salvage, and interventional radiological procedures should be considered. Antenatal diagnosis of placenta accreta is associated with less maternal and neonatal morbidity including decreased blood loss at delivery and transfusion of fewer units of blood products. Ultrasonography is a useful screening procedure but may be imperfectly sensitive/specific. MRI may help in such patient.

Unanticipated MOH
Bonnar describes a five-step management plan for MOH.\textsuperscript{22}
1. Organization of multidisciplinary team
2. Restoration of blood volume
3. Correction of defective coagulation
4. Evaluation of response to treatment
5. Treating the underlying cause of bleeding.

Communication and teamwork are essential in case of both anticipated and unanticipated MOH.

Steps of management include:
- Alerting blood transfusion service and hematologist.
- Ensuring the availability of O negative, 2-4 units of blood for emergency use. Allocation of roles to the team members is essential for the effective management.
- Assessment of airways, breathing and circulation in accordance with advanced life support guidelines.\textsuperscript{15}
- Attach monitoring lines, BP, electrocardiography, oxygen saturation.
- Give high flow oxygen via face mask with a reservoir bag.
- Head down tilt to increase the venous return and preserve cardiac output.
- Intravenous access with two large bore cannulae and take blood for cross matching.
- Foley’s catheter to monitor urine output.
- Consider arterial cannulation for arterial blood gas, invasive monitoring of BP and blood samples for evaluation of coagulation.
- Fluid resuscitation gives warm crystalloids up to 2 L (ringer lactate, normal saline) with rapid infuser or pressure bags and colloids up to 1-2 L until blood arrives.
- Large volumes of cold fluids place the patients at risk of hypothermia which induces shivering and subsequently increases oxygen consumption in a patient with already decreased oxygen carrying capacity and decreased oxygen reserves. Hypothermia also impairs coagulation, affects renal and liver function and delays wound healing.

Prompt communication between anesthesiologist, obstetrician and gynecologist, nursing and laboratory staff and blood bank is essential for effective evaluation and management of excessive blood loss.
**Coagulopathies in Pregnancy**

*Pathophysiology*

The etiology of coagulopathy in obstetrical hemorrhage may be due to dilutional coagulopathy, localized consumption, disseminated consumption, and increased fibrinolysis.23

Other than obstetric causes of coagulopathy in pregnancy (abruptio placenta, preeclampsia), bleeding disorders should also be kept in mind as an important differential diagnosis. PPH may be the first indication in patient suffering from Von Willebrand disease. A patient with menorrhagia when screened in antenatal care may be timely diagnosed for such types of bleeding diathesis.2

**Biomarkers to diagnose coagulopathy of pregnancy**

Hypercoagulable state of pregnancy is marked by increases in fibrinogen concentration, Von Willebrand Factor, F VII, FVIII and FIX concentrations.24

1. Fibrinogen: Fibrinogen levels fall below normal pregnancy range sooner than other coagulation factors,25 and in some circumstances may rapidly fall to <2 g/l in PPH. There is strong evidence that a low claus fibrinogen is an accurate biomarker for progression from moderate to severe PPH.26

2. Rotational thromboelastometry (ROTEM) and TEG: Current evidence suggests that targeted goal-directed therapy using coagulation factor concentrates guided by visco-elastic methods such as ROTEM or TEG enables the effective correction of coagulopathy and is associated with a decreased incidence of allogenic blood transfusion and thrombotic/thromboembolic events and with reduced costs.27

There are many limitations of coagulation monitoring using TEG and ROTEM. By direct addition of an activator, such as tissue factor or kaolin ROTEM and TEG automatically bypasses primary hemostasis and therefore cannot detect disorders of primary hemostasis. Most viscoelastic tests also cannot diagnose the cause of coagulopathy involving platelet function defects, for example, abnormal/deficient platelets due to antiplatelet drugs such as clopidogrel.28 Parallel assessment using point of care testing (POC) platelet function essays may, therefore, improve diagnosis.

3. ROTEM FIBTEM A5 assay: There is good evidence that the ROTEM FIBTEM A5 assay (available within 10 min) can be used as a surrogate for claus fibrinogen during PPH.29 This assay does not measure the same hemostatic parameter as claus fibrinogen but provides similar measures of hemostatic competence.28 As a rough guide, an FIBTEM A5 of 15 min equates to a claus fibrinogen of about 3 g/L; 10 min to 2 g/L and 6 min to 1 g/L.

A recent audit of an algorithm to manage obstetric hemorrhage (>1500 ml and ongoing) based on FIBTEM A5 has been published. It showed that the use of fibrinogen concentrate in place of fresh frozen plasma (FFP)/platelet “shock packs” when the FIBTEM A5 fell below 7 mm (and considered if below 12 mm in clinically severe bleeding), led to a substantial reduction in transfused red cells, FFP, cryoprecipitate, platelets and transfusion-associated circulatory overload and a nonsignificant reduction in hysterectomy.29 These data support the use of POC testing during PPH and provide evidence for a potentially appropriate intervention trigger (FIBTEM <12 mm and/or fibrinogen of 2.2 g/L). If the bleeding has stopped, the hemostatic blood products need not be given whatever the results. Unmonitored use of shock packs is unlikely to be beneficial for the majority of women.29 (Figure 1)

**CONSERVATIVE MANAGEMENT-UTEROTONIC DRUGS**

Uterotonic drugs such as oxytocin, ergotamine, methyl ergot, and 15-methyl Prostaglandin F2α are used.

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Figure 1: Point of care FIBTEM algorithm used at the University hospital of Wales in 2014. Reproduced with permission from author.
Misoprostol, a prostaglandin E1 analog has shown great promise as an uterotonic agent. In a study rectal administration of 1000µg of misoprostol lead to sustained uterine contraction and control of hemorrhage within 3 min.\textsuperscript{30}

**Invasive Management**

These are needed to be performed promptly in cases of failure of conservative management.

1. **Intrauterine balloon tamponade:**
   - Sengestaken Blakemore esophageal catheter is most often used. The catheter is inserted in the uterine cavity and balloon is filled with warm sterile water/saline until uterus is firm on palpation and bleeding is arrested. This technique is least invasive, most rapid, and lacks significant complications.\textsuperscript{31}

2. **Uterine compression sutures-(b-lynch sutures):**
   - They are most useful in refractory uterine atony.\textsuperscript{31}
   - Advantages include high success rate, ease of placement and fertility preservation.\textsuperscript{32}

3. **Angiographic arterial embolization-interventional radiology:**
   - Uterine artery and ovarian artery contribute significantly to uterine blood flow during pregnancy.\textsuperscript{31}
   - Embolization of these arteries with angiographic occlusion balloon catheters requires fluoroscopic guidance and expert interventional radiologist.\textsuperscript{32,33}
   - The patient should be stable enough to be transferred to radiological unit and monitoring should continue along with the facility to proceed with the surgical intervention if the patient becomes unstable.

4. **Arterial ligation:**
   - Surgical ligation of uterine, ovarian and internal iliac artery is useful when above methods have failed. Ligation of bilateral uterine arteries is easier than internal iliac artery ligation.\textsuperscript{34}

5. **Hysterectomy:**
   - Hysterectomy is a definitive treatment for PPH resulting from uterine atony and placenta accrete.\textsuperscript{33}
   - Peripartum hysterectomy is estimated to occur in 0.8/1000 deliveries.\textsuperscript{13}
   - If alternative interventions fail and bleeding continues, hysterectomy should not be delayed.

**TRANSFUSION OF BLOOD AND BLOOD PRODUCTS**

According to British Committee for Standards in Hematology, the therapeutic aim for the management of massive blood loss is to maintain.\textsuperscript{33}

1. Hemoglobin $\geq 7.5 \times 10^9$/L
2. Platelet count $\geq 75 \times 10^9$/L
3. Prothrombin time $\leq 1.5$ mean control
4. Activated prothrombin time $\leq 1.5$ mean control
5. Fibrinogen $\geq 1.0$ g/dl

**Cryoprecipitate**

It contains a higher concentration of fibrinogen than FFP. Existing risk of immunological reactions and the transmission of infectious agents have led to its withdrawal in several European countries.\textsuperscript{35} In the setting of PPH, cryoprecipitate is used to replace fibrinogen, which is rapidly consumed during obstetric hemorrhage. Guidelines recommend the use of cryoprecipitate to maintain the fibrinogen level above 1-1.5 g/L if FFP has not been successful.\textsuperscript{36,37} Cryoprecipitate has been shown to successfully increase fibrinogen levels during PPH.\textsuperscript{38}

One pool (1 bag of cryoprecipitate contains 325 mg of fibrinogen. 5 bags make one pool or 1625 mg of fibrinogen) of cryoprecipitate is expected to raise the fibrinogen level by about 0.5 g/L in the average women although this will vary depending on consumption. Cryoprecipitate also contains a high concentrate of factor VIII, Von Willibrand factor and factor XIII, which will be depleted in established hemostatic failure.\textsuperscript{35}

Dose of fibrinogen = (desired increase in g/L) $\times$ (plasma volume in L).

Thus, administration of 3 g of fibrinogen concentrate in a 70 kg patient increases the plasma fibrinogen concentration by 1.0 g/L (assuming 0.04 L/kg plasma volume) approximately.\textsuperscript{39}

**Platelets**

Guidelines recommend that the platelet count should be kept $>(50 \times 10^9)$\textsuperscript{3} during ongoing PPH and to achieve this they should be infused when the count falls below $(75 \times 10^9)$\textsuperscript{1}. With the exception of placental abruption, amniotic fluid embolus, severe preeclampsia or inherited or immune thrombocytopenia, a platelet count < $(75 \times 10^9)$\textsuperscript{4} is common during PPH. The strategy of 1:1:1 of red cells: FFP: Platelet transfusion would result in multiple platelet transfusions well above recommended levels and cannot be justified on current evidence.

**FFP**

In some centers red cells: FFP: Platelets are advocated into a 1:1:1 protocol.\textsuperscript{40} The products are frequently issued as “shock packs” on activation of a major obstetric hemorrhage protocol. The rationale for this approach is to maintain thrombin generation and fibrinogen by the replacement of coagulation factors as early as possible, and that it takes too long in practice to obtain lab results and issue components. The disadvantage of unmonitored “shock packs” is that the majority of woman will have completely normal coagulation and platelets at the time of
administration and will be receiving blood products with less fibrinogen and other coagulation factors than they have circulating. FFP is donated from nonpregnant population and has fibrinogen level of around 2 g/L and will therefore lead to reduction in fibrinogen, factor VIII, and Von Willebrand factor due to coagulation. Early empirical FFP may be justified if significant consumption is likely (e.g., placental abruption or amniotic fluid embolus), or very large volume of blood loss is expected (e.g., uterine rupture or placenta accreta). By contrast uterine atony or surgical/ genital tract trauma are unlikely to have early hemostatic impairment and early unmonitored FFP administration is more difficult to justify.\textsuperscript{25}

\textbf{VII a}

Recombinant factor VIIa (rVIIa) is not the first line treatment for hemorrhage and is effective only once major source of bleeding have been controlled. Before administration patient should ideally have platelet count 20,000/mm\textsuperscript{3}, fibrinogen >1 g/dl, temperature >32°C, pH >7.2, and normal ionized calcium. These preconditions will facilitate adequate functioning of clotting cascade. Optimal dose in obstetric hemorrhage is unknown though dose of 90 mg/kg is used.\textsuperscript{13} Despite having a very short half-life, (2-6 h), concerns about thromboembolism with factor VIIa as a complication are real. A recent systematic review showed a higher risk of arterial thrombosis (not venous) among patients who received factor VII as an adjunct therapy for life-threatening bleeding.\textsuperscript{41} It is recommended to give deep vein thrombosis (DVT) prophylaxis once the bleeding risk is considered to be low.

Seighton \textit{et al.} advise against rVIIIa administration in the setting of amniotic fluid embolism because tissue factor may play a role in its pathophysiology and thrombotic complications may be increased.\textsuperscript{42} The ASA guidelines recommended considerations of rVIIIa therapy of traditional well-tested options for treating microvascular bleeding (i.e., coagulopathy) have been exhausted.\textsuperscript{43}

\textbf{Tranexamic ACID}

This has been shown to reduce bleeding and transfusion requirement in massive hemorrhage secondary to a number of non-obstetric causes. Its role in obstetric bleeding is not established.\textsuperscript{44}

The WOMAN trial (world maternal antifibrinolytic) is currently attempting to further assess the role of antifibrinolytic therapy in post-partum hemorrhage. This randomized and double-blinded trial started recruitment worldwide in 2009 in a design similar to the CRASH 2 trial in trauma. The trial has recruited >4000 women to date and is aiming for a total of 15,000. This data set should be able to elucidate the impact of tranexamic acid on mortality and morbidity of postpartum hemorrhage and possible complications. Furthermore, it includes developing countries where the need for a pragmatic and cost-effective treatment of post-partum hemorrhage is greatest.\textsuperscript{45}

At present, the evidence for antifibrinolitics in obstetrics is limited. The EXADELI trial suggests a benefit of tranexamic acid in ongoing postpartum hemorrhage after vaginal delivery. There may also be a reduction in blood loss by prophylactic administration of tranexamic acid after cesarean section.\textsuperscript{45} Tranexamic acid may be most beneficial for women who demonstrate hyperfibrinolysis based on hemostatic monitoring such as TEG.\textsuperscript{27,46}

\textbf{Intraoperative Cell Salvage (IOCS)}

IOCS is now an established technique in the management of hemorrhage complicating cesarean section. IOCS was adopted late in obstetrics relative to other surgical interventions as a result of concerns regarding the potential for harvest and retransfusion of amniotic fluid causing so-called “amniotic fluid embolus.” But now, it has been proved that these fears were unfounded and that amniotic fluid is effectively removed by the salvage process and administration via a leukocyte depletion filter (LDF). Indeed use of a LDF and the requirement for dedicated suction for blood have not been questioned and abandoned by some advocates of technology.\textsuperscript{47} Furthermore, authors have stated that reinfusion of blood harvested by cell salvage and passage through LDF, results in clinically insignificant bacteremia. Further LDFs are also known to remove bacteria from blood.\textsuperscript{47} IOCS for autologous transfusion is already being used in cardiac, orthopedic and vascular surgeries with relative reduction of blood transfusion by 39% and absolute risk reduction by 23%.\textsuperscript{1} The use of IOCS has an undisputed role in patients who refuse blood or blood components transfusion (Jehovah’s witness) and in patients where massive blood loss is anticipated (placenta accreta, percreta).\textsuperscript{2} This technique can also reduce exposure to allogenic blood transfusion along with its risks as well as is cost-effective.

\textbf{Blood Conservation Strategies}

Autologous blood transfusion (donation, storage, and retransfusion) has been shown to be safe in pregnancy. Autologous transfusion is generally reserved for situations with a high chance of transfusion in a patient with rare antibodies.\textsuperscript{48,49} Early identification of patients at risk for obstetric hemorrhage and storage of autologous blood has been attempted for pre-operative autologous blood donation. Since most patients do not have identifiable risk factors and many patients do not donate more than one unit
of blood, its utility in acute severe hemorrhage is uncertain. Its utility and safety however have been questioned as it may cause anemia, does not eliminate transfusion risks and cannot be used in an emergency.\textsuperscript{[30]} It also subtracts the potential risks of homologous transfusions is cost-effective and decreases dependence on donors.\textsuperscript{[4]} It is important to identify women who refuse blood or blood product transfusion. For example, Jehovah's witness in which autologous transfusion is the only option.\textsuperscript{[51]}

Anesthesia Concerns in Patients with MOH

Senior anesthesiologist and intensive care team should be involved early as obstetric patients with severe hemorrhage may decompensate rapidly.

The focus of resuscitation should be the preservation of the woman's life rather than preservation of her uterus.\textsuperscript{[15]}

- Continue resuscitation with warmed fluids and avoid hypothermia.
- Consider arterial line, central line and urinary catheter but only after definitive treatment has commenced. Their insertion must not delay resuscitation and fluid management.\textsuperscript{[1]}
- The choice of anesthetic technique depends on the indication and urgency for delivery (as in the case of APH) the severity of maternal hypovolemia and the obstetric history, e.g., prior caesarean delivery.\textsuperscript{[3]}
- The main aims of management are rapid resuscitation to restore tissue oxygen delivery while predicting, preventing, and correcting hemostatic disorders.
- The presence of cardiovascular instability is a relative contraindication to regional anesthesia. Blockage of the sympathetic system can potentially lead to worsening of hypotension due to hemorrhage. If cardiovascular stability has been achieved and there is no evidence of coagulation failure regional anesthesia can be used.\textsuperscript{[56]}

This may be particularly appropriate where a working epidural block has been in place during labor. Continuous epidural block is preferred over spinal as it allows better control of BP and can be used for prolonged surgery.

If surgery is required, one should remember to ensure that routine safety precautions are taken including anesthetic history, airway assessment, antacid prophylaxis, and preoxygenation.\textsuperscript{[15]}

General anesthesia following a rapid sequence induction with cricoid pressure is the technique of choice in hemodynamically unstable patients.\textsuperscript{[15]}

Etomidate or ketamine may be preferable to thiopentone or propofol in the presence of severe hypovolemia.\textsuperscript{[4]} Ketamine 0.5-1.0 mg/kg has an excellent record of safety and efficacy in obstetric anesthesia practice.\textsuperscript{[5]}

The volatile agents cause uterine relaxation and excessive concentrations should be avoided especially in the case of uterine atony.\textsuperscript{[15]}

- Regular monitoring of hemoglobin level and coagulation using near patient devices if available (e.g., hemacue). FFP, platelets, transfusion, and cryoprecipitate may be necessary if coagulopathy develops. Early liaison with hematology department for optimal and timely blood product replacement is of utmost importance.
- Perioperative monitoring of all vital parameter and recording of this parameter on a flow chart such as the modified obstetric early warning system charts.\textsuperscript{[1]}
- There is a consensus that fibrinolytic inhibitors seldom if ever have a place in the management of obstetric hemorrhage.
- Post-operative management includes transfer to intensive care unit/high dependency unit.
- Anticipate coagulopathy and treat clinically until coagulation results are available.
- Once the bleeding is arrested and any coagulopathy is corrected, thromboprophylaxis is administered as there is a high risk of thrombosis.
- Pneumatic compression devices can be used if thromboprophylaxis is contraindicated in cases of thrombocytopenia.

CONCLUSION

Obstetric hemorrhage is the most common cause of maternal morbidity worldwide and a leading contributor to the maternal mortality in developing nations. Major obstetric hemorrhage is managed by multidisciplinary approach. Clinicians should identify risk factors before and during labor so that the care may be optimized for high-risk women. Team responses that emphasize the accurate estimation of blood loss, early warning signs of shock and rapid response to blood loss and coagulopathy, a clear cut protocol are associated with less maternal morbidity. Urgent access to definitive care remains a major stumbling block in limited resource areas in the developing world. However, recent advances in prediction and assessment of blood loss, a better understanding of coagulation mechanisms, POC monitoring and the availability of minimum trading price should improve the efficacy of management of MOH. Central to success is the flair and leadership skills of anesthesiologist in coordination of
resuscitation and communication among team members. POC testing using viscoelastic methods such as ROTEM or TEG should be performed to guide the rapid identification of specific coagulation disorders and more accurate evaluation of coagulation. The role of tranexamic acid in obstetric hemorrhage is yet to be established. The guidance however will need to be updated as on-going clinical trials are updated.

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Denture Adhesives in Prosthodontics: A Review

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Abstract
Denture adhesives have a long been recognized by the denture wearers as a useful adjunct to denture retention and stability. Several studies reported that the denture adhesives are effective in increasing the retention of complete dentures, regardless of their brand or form. Although denture adhesives were used in the later part of the 18th century, they were not acknowledged in the dental literature until 1930’s. The long-term use of denture adhesives without professional advice is contraindicated for many reasons. This review report discusses the review of literature, indications, mode of application, and contraindications for the use of denture adhesives.

Key words: Adherents, Denture adhesives, Denture retention, Fixatives

INTRODUCTION
Contrary to the negative approach toward denture adhesives, their use can be a justifiable, therapeutic, effective augmentative procedure in denture fabrication, and treatment plan.¹ The main active components in today’s denture adhesives are a blend of polymer salts with various degrees of water solubility. The desired attributes of a denture fixative are sensitivity to hydration, rapid onset of action, sufficient duration of action, washout resistance, and ease of cleansibility.² Dental professionals have been slow to accept the use of dental adhesives for denture retention, despite the knowledge that the use of denture adherents is a fact of life for a large number of denture wearers.³ Patient comfort and ease of use are the major factors that influence a patient to select a particular denture adhesive product.⁴ Neill and Roberts, Fujimori et al. observed an increase in the masticatory efficiency of CD wearers by using different denture adhesives in comparison with control groups.⁵,⁶

REVIEW OF LITERATURE
Many researchers also have evaluated different aspects of denture adhesives in patients with well-fitting complete dentures.⁷-¹⁰ Although manufacturers’ instructions guide the patient, the experience of the patient with the adhesives influences its correct application. The use of denture adhesives began during the age of modern dentistry in the late 18th century.¹¹ The patent issued for the earliest adhesives was in 1913.¹² The early denture adhesives washed out readily from beneath the denture, rendering the fixative useful for only a relatively short period.¹²

Denture adhesives when properly used are beneficial to the patients in improved fit, comfort, function, and psychological security.¹³ An ideal denture adhesive should be nontoxic, biocompatible and nonirritating to the oral mucosa. It should not promote growth of microbes, and should be odorless, tasteless, and easy to administer and to remove from the tissue-bearing surface of prostheses.¹ The patients wearing dentures should be instructed to consult the dentist for periodic examinations of their prostheses and the health of the oral cavity. The two critical issues associated with the use of a denture adhesive is its efficacy in improving function and its effect on the health of the underlying oral tissues.¹⁴ Denture adhesives improve the digestion of complete denture wearers and let such patients to
chew foods of a harder consistency. Therefore, denture adhesives may improve the general health of complete denture wearers.\textsuperscript{15}

\textbf{MODE OF APPLICATION}\textsuperscript{2}

Several studies reported that the denture adhesives are effective in increasing the retention of complete dentures, regardless of their brand or form.\textsuperscript{16-19} Clean the food debris, saliva and residual adhesive material from the tissue-bearing surface of the denture. Apply small quantities of denture adhesive to the tissue bearing surfaces of the denture. Wet the denture ahead of applying the denture adhesive powder. Apply the adhesive to the anterior alveolar ridge, center of the hard palate, and posterior palatal seal regions of maxillary dentures and to the sulcus of the denture over the crest of the alveolar ridge extending from the anterior sulcus to the distal extension of mandibular dentures. After seating the denture, hold it firmly with hand pressure for 5-10 sec. Advise the patient to close the jaw into centric occlusion a few times to distribute the adhesive in a thin layer between the mucosa and denture base.

\textbf{INDICATIONS}\textsuperscript{2}

1. To stabilize trial bases
2. To augment retention and stability of immediate dentures
3. To secure an existing or interim prosthesis in patients undergoing intraoral surgical procedures
4. Psychologic support
5. Compromised anatomic structures
6. Elderly patients
7. Physically/mentally challenged patients
8. Xerostomia
9. New dentures
10. Osseointegrated implants

\textbf{CONTRAINDICATIONS}

Patients having allergy toward any of the components of denture adhesive should refrain from using it. Hedera \textit{et al.} evaluated the hypocupremic complete denture patients and observed that all patients studied with copper deficiency had ingested large amounts of zinc from denture adherents.\textsuperscript{20} Excessive zinc ingestion from the overuse of zinc-containing denture adhesives can cause elevation of serum zinc levels that result in reduction of serum copper which leads to bone marrow depression along with widespread sensory and motor neuropathies.\textsuperscript{21} The use of denture adhesive is contraindicated in patients with severe ill-fitting dentures, midline fractured maxillary dentures and in cases of pathology or tissue hyperplasia. Also long-term, the use of a denture adhesive without periodic professional advice is contraindicated.\textsuperscript{2}

\textbf{CONCLUSION}

Some dentists and patients consider denture adhesives a useful aid for denture retention and function, whereas others observe them as a poor substitute for a proper fitting denture. The denture adhesive when used properly should provide comfort, sufficient retention and stability to the denture, ensuring the patient’s ability to function with freedom during speech, chewing and smiling. Dentists need to explain the need for periodical denture relining procedure to minimize the use of denture adhesives. The advantages of implants on denture stability should also be stressed.

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Carbimazole-induced Cholestatic Hepatitis in Toxic Multinodular Goiter

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Abstract
Antithyroid drugs are the treatment option for toxic multinodular goiter. Carbimazole is usually the drug of choice except in pregnancy where propylthiouracil is used. It is well tolerated and common side effects include allergy, upper GI upset, and rarely agranulocytosis. Hepatitis is another rare but serious complication. Hereby, we report a case of 55 years female with toxic nodular goiter, who developed cholestatic hepatitis after carbimazole therapy for 2 months. She recovered completely following withdrawal of the drug.

Key words: Carbimazole, Cholestatic hepatitis, Toxic multinodular jaundice

INTRODUCTION
Toxic multinodular goiter (Plummer's disease) is the 2nd most common cause for hyperthyroidism after Grave's disease. It accounts for 15-30% cases. Toxic nodular goiter (TNG) is more common in elderly (>50 years) and in women. Unlike Grave's disease which is autoimmune and antithyroid are started universally, TNG is not known to recur after therapy. Hence, surgery or radioiodine is the treatment of choice. Antithyroid is still used for symptomatic relief in patients waiting for surgery. It has several side effects the majority are mild and include allergic reactions and upper GI intolerance. Other side effects include agranulocytosis and vasculitis-like reaction particularly with propylthiouracil (PTU). Hepatotoxicity is rare, but serious side effects with both carbimazole and PTU. Fatal cases have been documented with both drugs. The hepatic histology with PTU is toxic hepatitis and necrosis and it is cholestatic hepatitis with carbimazole. We present a case of carbimazole-induced cholestatic hepatitis in a patient with TNG. Clinical and biochemical findings in this patient with relevant review of literature are presented.

CASE REPORT
A 55-year-old female patient presented to the surgical outpatient department with chief complaints of progressive swelling over the neck for the last 10 years which has become symptomatic in the form of difficulty in swallowing for the last 4 months. She also has associated complaints of palpitations, weight loss of 5 kg and bilateral bulging eyes. There were no associated comorbidities. No h/o liver disease. She had no history of any addiction. On examination, her weight was 50 kg. She had a pulse rate of 112/min, regular; B.P was 140/85 mmHg. Ophthalmic examination showed bilateral exophthalmos. Systemic examination was normal. Thyroid swelling measured 8 x 6 cm, which was firm nontender with nodular surface and no bruise, was heard.

Her initial T4 was 23.1 µg/dl, T3-2.56 ng/dl and thyroid stimulating hormone <0.01. She was diagnosed as a case of toxic multinodular goiter and discharged on tablet propranolol 40 mg daily and carbimazole 40 mg/day. I 131 was not started as fear of exacerbating eye manifestations was there. However, she re-presented 4 weeks later with progressively deepening jaundice, pruritus, and passage of clay-colored stools. There was no previous history of jaundice, blood transfusions, intravenous drug abuse, anesthesia, recent history of travel, or animal exposure. She was markedly jaundiced on examination. There were no peripheral stigmata of chronic liver disease. There was no right hypochondrial tenderness, hepatomegaly, features of
hepatic encephalopathy, or cardiac decompensation. Results of the liver function tests are shown in the table. The lab findings were suggestive of cholestatic jaundice. Her serology was negative for hepatitis A anti-IgM antibody, hepatitis B surface antigen, hepatitis B core anti-IgM, hepatitis B surface anti-IgM, hepatitis B antigen, and hepatitis C virus anti-IgM. Her ANA, AMA, and anti-LKM antibodies were negative. The abdominal ultrasound demonstrated a normal sized liver with no focal lesions. The bile ducts, pancreas, kidney, and spleen were all reported as normal. Contrast-enhanced computed tomography abdomen and magnetic resonance cholangiopancreatography did not reveal any obstruction in the biliary tract. A liver biopsy was undertaken once contraindications to the procedure (such as derangements in coagulation profile) had been excluded which showed intrahepatic cholestasis. Carbimazole was stopped suspecting a drug-induced pathology and follow-up Liver function tests (LFTs) were done.

The patient is was put on propranolol and prednisolone in the interim for her thyrotoxicosis and exophthalmoses. Her liver function tests improved significantly following stoppage of carbimazole. The high degree of alkaline phosphatase could also be due to the effect of hyperthyroidism on bone resorption. She is currently euthyroid (Figures 1-4 and Table 1).

Table 1: Serial LFT reports showing her course of illness

<table>
<thead>
<tr>
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<tbody>
<tr>
<td>Serum bilirubin total (mg/dl)</td>
<td>0.3-1.3</td>
<td>27.6</td>
<td>25.4</td>
<td>20.6</td>
<td>11.6</td>
<td>4.5</td>
</tr>
<tr>
<td>Serum bilirubin direct (mg/dl)</td>
<td>0.1-0.4</td>
<td>17.4</td>
<td>16.8</td>
<td>14.38</td>
<td>7.54</td>
<td>2.1</td>
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<tr>
<td>SGOT (U/L)</td>
<td>12-38</td>
<td>165</td>
<td>112</td>
<td>96</td>
<td>65</td>
<td>45</td>
</tr>
<tr>
<td>SGPT (U/L)</td>
<td>7-41</td>
<td>112</td>
<td>100</td>
<td>88</td>
<td>59</td>
<td>44</td>
</tr>
<tr>
<td>Serum protein (U/L)</td>
<td>7-9</td>
<td>5.3</td>
<td>6.4</td>
<td>6.3</td>
<td>6.4</td>
<td>6.6</td>
</tr>
<tr>
<td>Serum albumin (U/L)</td>
<td>4-6</td>
<td>3.3</td>
<td>3.8</td>
<td>3.3</td>
<td>3.6</td>
<td>3.8</td>
</tr>
<tr>
<td>Alk phosphatase (U/L)</td>
<td>4-126</td>
<td>2300</td>
<td>2215</td>
<td>1732</td>
<td>1164</td>
<td>668</td>
</tr>
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SGOT: Serum glutamic oxaloacetic transaminase, SGPT: Serum glutamate-pyruvate transaminase, LFT: Liver function tests
DISCUSSION

Thyroid dysfunction may perturb liver function, and the liver modulates thyroid hormone metabolism. A variety of systemic diseases and drugs may affect both organs.\(^1\,^2\)

Thyrotoxicosis and Hepatobiliary Injury

Abnormal liver biochemical test results have been reported in hyperthyroid patients before and after antithyroid therapy. Gurlek et al.\(^3\) showed that 60.5\% of 43 patients with hyperthyroidism had at least one liver abnormality at diagnosis. Hepatic damage occurring from thyrotoxicosis per se has been ascribed to ischemic injury resulting from a relative decrease in blood flow despite increased metabolic activity of the liver.\(^1\) But bear in mind that raised alkaline phosphatase may not be of liver origin but rather from bone, indicating an osteoblastic response to thyroid hormone-induced bone resorption.

The nature of hepatic injury caused by thionamides is dependent on the specific drug. While carbimazole and its active metabolite methimazole typically cause cholestasis, PTU is notable for causing hepatocellular injury.\(^4\,^7\) Thionamide-induced liver damage is an idiosyncratic reaction that can develop at any time, but usually occurs within the first 3 months of treatment. It occurs in about 1\% of patients with a predisposition for women younger than 30 years of age.\(^1\) The mechanism of injury is thought to be based on an allergic host response.\(^1\,^4\,^8\)

Our patient had a predominantly cholestatic hepatitis, which is consistent with cases of carbimazole- and methimazole-induced hepatic damage reported in the literature.\(^9\,^11\) Thionamide therapy may be an additional insult to the liver. Ai-Leng et al.\(^12\) reported a case of fatal hepatic failure in a patient on carbimazole and bupropion, while Enghofer et al.\(^13\) reported fulminant hepatitis A infection in a hyperthyroid patient treated with carbimazole. Therefore, we suggest that it might be prudent to exclude additional risk factors for the liver injury in patients presenting with thionamide-associated cholestasis.

Our patient developed significant hyperbilirubinemia within 4 weeks of starting therapy with significant elevation of alkaline phosphatase. The aminotransferases were mildly elevated, reaching two-three times the normal. She showed good response to withdrawal of drug and is currently doing well. Cholestatic hepatitis developing due to carbimazole in TNG has not been described in the past and has only been described in patients with Grave’s disease.\(^14\,^15\)

CONCLUSION

- Jaundice as a complication of thionamide treatment of hyperthyroidism is rare.
- This complication cannot be predicted by deranged liver enzymes at presentation, but typically occurs within 3 months of therapy.
- It can be fatal, particularly when there are additional hepatotoxic factors.
- The drug must be withdrawn immediately and alternative therapy for hyperthyroidism, such as radioiodine must be considered in appropriate patients.

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Aggressive (Deep) Angiomyxoma of Vagina: A Rare Case Report

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INTRODUCTION

Case of aggressive angiomyxoma (AAM) was first described as a distinct clinicopathologic entity by Steeper and Rosai in 1983.1 AAM is a rare tumor of mesenchymal origin. About 90% of the patients are women in reproductive age group with a peak incidence between the 3rd and 4th decades of life.1

AAM usually arises in deep soft tissue of the vulvo-vaginal region, perineum, pelvis of young adult females and analogous sites including scrotum and the inguinal area in males.2 It is a slow growing tumor but problematic due to frequent local recurrence (30-72%).2 Female to male ratio is 6.6:1.4 However, metastasis is very uncommon.4 Misdiagnosis is a very frequent problem.3 Diagnosis is mostly made on histopathology following surgical resection.3

We report a case of AAM in 45-year-old pre-menopausal female presenting with a vaginal mass on anterior vaginal wall.

CASE REPORT

A 45-year-old premenopausal female patient, para2live2, visited to gynecology outpatient department with complaints of a painless mass in the vagina gradually increasing in size over the last 8 years, now protruding out of the vagina and dyspareunia since the last 1 year. The patient had no relief of the symptoms on seeking medical advice from the local practitioner. No bladder or bowel complaints.

Menstrual History

Past menstrual cycles were regular. Last menstrual period was 7ss before.
Obstetrical History
Para 2 live, all full term normal delivery, last child birth 14 years before.

General and Systemic Examination
The patient was averagely built, afebrile, pulse was regular, mild pallor, and no icterus. Cardiovascular and respiratory system revealed no abnormality, per abdomen soft with no guarding and rigidity. No systemic signs of thyroid disorder found on examination.

Local clinical examination revealed a well-defined firm irregular mass of 7 cm × 6 cm × 5 cm, which was non tender, arising from anterior vaginal wall in the suburethral region, 4 cm below the urethral meatus with the wide base as shown in Figure 1. Posterior vaginal wall and cervix were healthy as seen in Figure 2. Uterus was anteverted and normal size, fornices free and non tender, per rectal examination revealed no mucosal involvement.

Investogram
Her investigations revealed hemoglobin: 11.8 g/dl, total white blood cell count (total leukocyte count): 12,680/cumm, platelet: 4.2 lakhs/cumm, serum bilirubin: 0.6 mg/dl, blood sugar random: 104 mg/dl, serum glutamic-oxaloacetic transaminase: 26 IU/L, serum glutamate pyruvate transaminase: 25 IU/L, blood urea: 29 mg/dl, and serum creatinine: 1 mg/dl. HIV and hepatitis B surface antigen were nonreactive. X-ray chest was within normal. Histopathology report of the pre-operative biopsy (done twice) showed inflammatory changes with no tissue diagnosis. Contrast-enhanced computed tomography (CECT) was performed for better characterization and the extension of tumor. It revealed an ill-defined heterogeneously enhancing soft tissue mass lesion of size 10.5 cm × 5.3 cm × 7.8 cm, arising from anterior vaginal wall, extending inferiorly in subcutaneous plane in the vulval region. Superiorly extending up to anterior lip of cervix. Fat planes between this mass and bladder were well maintained. Hence, surgery was planned after evaluation for possibility bladder involvement by the surgeons.

Procedure Performed
Removal of the vaginal mass was done in the lithotomy position. Under spinal anesthesia per speculum and per vaginal examination were done to confirm pre-operative findings. The patient was catheterized to facilitate the surgery and to prevent trauma to urethra. Mass was identified 4 cm below from urethral meatus. To develop the tissue planes normal saline was infiltrated around the mass, and the circumferential incision was taken at the base of mass (bladder approximately 2.5 cm away from the mass). The base of the pedicle was separated with sharp dissection, and the base of mass was dissected from the vaginal wall in the region of the pedicle. The dissection was easy. The base of the pedicle was reached posterior to symphysis pubis. The base of the pedicle was clamped as close to the hind surface of the symphysis pubis and the polyp growth was removed. At the end of the procedure, there was no visible or residual palpable mass. Hemostasis was achieved and the incision was closed with 2-0 vicryl. Vagina was packed and the pack was removed after 24 h catheter was removed after 7 days.

On gross examination, the mass was well circumscribed measuring 8 cm × 8 cm × 7 cm in size (Figures 3 and 4) and weighing 65 g.

On cut section, it appeared gelatinous, glistening, and bluish-gray.

On histopathology, hematoxylin and eosin stain revealed tumor tissue composed of small and large vessels lined by endothelium surrounded by smooth muscle coat with myxomatous stroma. Tumor covered with thin layer of epidermis with fairly uniform, moderate cellularity containing small, stellate-shaped and spindled cells, in myxomatous stroma suggesting angiomyxoma (Figures 5).
Immunohistochemistry was not done in this case as the patient was poor and at Government Medical College and Hospital, Aurangabad, this test is not available.

Post-operative patient was observed in the hospital for bleeding and urinary leaks for 7 days and was treated with prophylactic antibiotics. The follow-up was uneventful with no signs of recurrence (Figure 6).

**Histopathology**

Histopathology revealed thin uniform epidermis, small and large vessels lined by endothelium surrounded by smooth muscle coat. Stroma is myxomatous spindle and stellate cells seen (Figures 7 and 8).

**DISCUSSION**

The term AAM was coined by Steeper and Rosai in 1983 for a morphologically distinctive, slow growing, myxoid neoplasm that occurs mainly in genital, perineal, and pelvic
region of adult women. It is of two types as follows:
1. Superficial which grows near surface
2. Aggressive which grows and invades in deeper tissues and has tendency for recurrence, 90% of patients are in reproductive age group.

The patient usually presents with noticeable mass and rarely has pain. The initial presentation varies from asymptomatic perineal or vulval nodule or polyp or perineal hernia to a pelvic mass diagnosed on imaging study. In this case, premenopausal patient presented with painless mass increased in size over the last 8 years. Occasionally, tumor can be cystic and mistaken for Bartholin's, labial, or gartner duct cyst. The tumor characteristically grows slowly and insidiously. It usually takes 2 months to 17 years for patient to report to the hospital.

Genetics
The pathogenesis of the AAM is poorly understood; however, genetic alterations along the 12 q chromosome region chromosomal abnormality involving chromosome 12q 13-15 have been implicated. These translocations involve high mobility Group A protein (high-mobility group AT-hook 2 [HMGA2]). HMGA2 belongs to a family of transcription factor that function during embryogenesis and usually not detected in adult tissues. Cytogenetic analysis and fluorescent in situ hybridization have confirmed the presence of HMGA2 gene in the rearrangement in AAM.

Immunohistochemically, most AAM express different combinations of estrogen and progesterone receptors and show immunopositivity for vimentin, desmin, smooth muscle actin, muscle specific actin, CD 34, and CD 44. They showed strong immunoreactivity for actin but were negative for S-100 protein.

Immunohistochemistry, in this case, was not done as the patient was poor and test is not available in Government Medical College, Aurangabad.

Gross Appearance
Tumor size ranges from 3 to 60 cm, it can appear as polypoid, soft, bulky mass, or vaginal cyst. External surface is smooth and usually neither encapsulated nor circumscribed. It has gelatinous consistency with focal areas of congestion and hemorrhage on cut section. It is usually homogeneous in consistency with no obvious nodularity.

On gross examination, in this case, the mass was well circumscribed measuring 8 cm × 8 cm × 7 cm in size.

On cut section, it appeared gelatinous, glistening, and bluish-gray.

Microscopic Appearance
Spindle stellate cells separated with loose myxoid stroma focally rich in collagen fibrils, a prominent vascular component. Mitotic activity is extremely low. In this case, histopathology reveal revealed tumor tissue composed of small and large vessels lined by endothelium surrounded by smooth muscle coat with myxomatous stroma. Tumor covered with thin layer of epidermis with fairly uniform, moderate cellularity containing small, stellate-shaped and spindled cells, in myxomatous stroma suggesting angiomyxoma.

Scanning
Several imaging modalities have been used in identifying and describing AAM. Sonography usually reveals hypoechoic or cystic mass. CTs and magnetic resonance imaging (MRI) are useful in diagnosis and help in complete removal of tumor particularly arising in perineum, vulva, and bladder. AAM display unusual growth pattern with high signal density in T2 weighted MRI. MRI scan shows a “swirled” pattern visible in the angiomyxoma and is more specific than CT scan, so imaging study of choice for these lesions. In this case, CECT revealed an ill-defined heterogeneously enhancing soft tissue mass lesion of size 10.5 cm × 5.3 cm × 7.8 cm, arising from anterior vaginal wall, extending inferiorly in subcutaneous plane in the vulval region extending superiorly up to anterior lip of cervix. Fat planes between this mass and urinary bladder were well maintained.

Differential Diagnosis of AAM
- Angiomyofibroblastoma
- Bartholin gland cyst
- Vaginal polyp
- Leiomyoma
- Leiomyosarcoma
- Lymphangioma
- Malignant fibrohistiocytoma
- Myxolipoma
- Myxoid leiomyoma
- Myxoid neurofibroma
- Slerosing hemangioma.

Treatment and Prognosis
The first line of therapy for AAM is surgery, although achieving negative resection margins are difficult because of the infiltrative nature of tumor and the absence of defined capsule. Smaller and more superficial tumor of the vulva or vagina may be removed with the wide local excision, but larger, deep-seated tumors of the pelvis may require more extensive surgery with partial or complete resection of some pelvic organ. The recurrence rate is very high (>35%). Most of the AAM tumor shows estrogen and progesterone receptors and is likely to be hormone
dependent. Hormones can be given pre operatively to decrease tumor size. Pre-operative GnRH analogs has been used successfully in few instance in premenopausal women with AAM having positive estrogen and progesterone receptors. Pre-operative use of GnRH analog decreases the tumor size and makes the complete removal of the tumor feasible. Due to the low mitotic activity in these tumors radiotherapy and chemotherapy are of not much help. Angiographic embolisation has been attempted to shrink the tumor. Two cases of successful control of recurrent angiomyxoma with relatively high doses of external radiotherapy have also been reported. Two cases of metastasis had been reported in literature as follows: 1. Pulmonary and mediastinal metastasis 2. Metastasis to the lung.

Recurrence is one of the unique characteristics of these otherwise nonmalignant tumors. The usual sites of recurrence reflect the site of the primary disease, i.e., perineum, pelvis. No definite relation between patient's age, size of tumor and rate of recurrence has been established so far.

**CONCLUSION**

Many options for the treatment of recurrence such as repeat surgery radiotherapy and hormonal therapy have been tried with varying success, but no single modality is clearly beneficial over others. All patients need long-term follow-up, usually with the clinical examination and MRI to detect early recurrence. In our case, we resected the tumor with no visible or palpable residual tumor and there are no signs of recurrence after 3 months.
Atypical Presentation of Extra-follicular Adenomatoid Odontogenic Tumor of Anterior Maxilla: A Clinical Predicament

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Abstract

The adenomatoid odontogenic tumor (AOT) is a hamartomatous proliferation of odontogenic epithelium with slow growth potential constituting around 3% of all odontogenic tumors. The tumor has a more predilection for females in the second decade of life, involving the maxilla more commonly. The tumor present in three variants: Intra-follicular (73%), extrafollicular (24%), and peripheral (3%). We report a case of extra-follicular AOT in an 11-year-old male patient presenting with firm, painless swelling on the right anterior maxilla with respect to 11-12 tooth region without any relevant dental history leading to a provisional diagnosis of the developmental maxillary cyst. Fine needle aspiration revealed a benign neoplasm and histopathological examination along with radiographic correlation confirmed the diagnosis of an extra-follicular AOT of anterior maxilla.

Key words: Adenomatoid odontogenic tumor, Extra follicular, Fine needle aspiration cytology

INTRODUCTION

Adenomatoid odontogenic tumor (AOT) is an uncommon, expansile, hamartomatous and asymptomatic benign non-invasive lesion of odontogenic origin that was first described by Driebaldt in 1907 as a pseudo-adenoameloblastoma.¹ After some terminological controversy, the name “AOT” was first proposed by Philipsen and Birn in 1969,² and adopted by the World Health Organization (WHO) classification of odontogenic tumors in 1971.³ At present, it is recognized as AOC.⁴ Sometimes it has been referred to as two-thirds tumor.⁵

There are three clinical variants such as follicular variant (F) is intraosseous associated with impacted and displaced tooth; extra-follicular variant (Sub type-E1, E2, E3, E4) is within the bone but not associated with unerupted tooth rather in between erupted tooth mimicking a radicular cyst or lateral periodontal cyst; peripheral (epulis-like) variant (P) exhibits a periodontal bone defect or ectopic growth.⁶

Here, we reported a case of extra-follicular AOT of the maxilla, presenting as a maxillary cyst with the diagnostic challenge.

CASE REPORT

An 11-year-old male patients presented with a painless swelling over the upper anterior region with respect to 11-12 tooth region for 3 months. Swelling was gradual in onset with the displacement of adjacent tooth with time and reach to the present condition. There was no history of dental caries, pus discharge, and tooth mobility. There was no relevant medical history, and routine blood investigation was inconclusive.

On extra-oral examination revealed slight elevation of right upper lip region with minor obliteration of nasolabial fold, no sign of inflammation, and no lymphadenopathy. Intraoral examination showed solitary bulging from upper alveolus and attached gingiva measuring about 3 × 2 cm
with respect to 11-12 tooth region with palatal extension and thinning out of the labial cortical plate. There was displacement of a lateral and central incisor with remains vital. On palpation, swelling was diffuse, soft to firm in consistency, non-tender, non-pulsatile, non-fluctuant, and slightly compressible and showed no evidence of discharge on digital pressure (Figure 1a).

Intra oral periapical radiograph and orthopantomogram showed well-defined unilocular radiolucency in the interdental area with the destruction of alveolar bone with respect to 12-11 tooth region and loss of lamina dura of 12 teeth only (Figures 1b and c).

From clinico-radiological evidence leads to a provisional diagnosis of the developmental maxillary cyst.

Fine needle aspiration cytology (FNAC) of that lesion yielded clusters and sheets of basaloid cells with scanty to moderate cytoplasm having round-oval benign nuclei with fine chromatin and indistinct nuclei in a mucoid matrix and peripheral palisading also noted, imprinting a cytopathological diagnosis of benign neoplasm possibly of ameloblastoma or AOT or basal cell adenoma (Figures 2a and b).

Excisional biopsy was advised and gross specimen showed grayish black solitary nodule with a cystic cavity having whitish glistening proliferating mass filled up the cavity (Figure 2c). Microscopic examination revealed proliferative epithelium arranged in whorls, nests and ducts surrounded by columnar, cuboidal cells having eosinophilic material in the center within a loose connective tissue stroma surrounded by thick fibrous capsule (Figures 2d-f). The final diagnosis was made as AOT extra-follicular type (E2 type). The present case had uneventful healing with asymptomatic after 1-month follow-up (Figure 1d). The patient was advised for orthodontic consultation for the management of the tooth spacing.

**DISCUSSION**

AOT is a slow growing odontogenic tumor with variable growth potential. It occurs typically in young persons in the second or third decades with female predominance in a global incidence of 1.9:1 and for Asian 2.3:1.6 76% of cases found in the anterior part of the jaw with a marked maxillary preference of 4.5:2.5\(^6\) and commonly located in the lateral incisor, canine and premolar region. The present case was a young male patients presented as an unusual slow growing mass over right anterior maxilla in between central and lateral incisor.\(^7\)

It is frequently encountered as a painless intraosseous lesion with impacted canine.\(^4\) However, it may rarely occur in a normally erupted dentition as extra-follicular type and uncommonly as a peripheral type.\(^7\) The present case was not associated with impacted tooth and intra-radicular tumor location with roots divergence confirmed the diagnosis of extra-follicular E2 Type.

Radiologically, the tumor is well demarcated unilocular radiolucency, displacement of the adjacent tooth with least root resorption and sprinkle calcification which is not always sufficient to produce radiopacity.\(^4\) It is always misdiagnosed as dentigerous cyst, fissural cyst, lateral periodontal cyst, radicular cyst, and nasopalatine cyst in accordance to clinico-radiological interpretation.\(^7\)
Extra-follicular AOT is often misdiagnosed by clinician due to low incidence and uncommon presentation of the disease and should be confirmed by histopathological examination. According to a review of literature FNAC of AOT has not been practiced much. In our case, FNAC not only ruled out the cystic lesion but also suggested to a cytological diagnosis of benign neoplasms - such as basal cell adenoma, ameloblastoma, and AOT - which are rarely found in this location. This finding prompted us to explore the cytological diagnosis, and the patient was advised biopsy in follow.

The histological features in our case were consistent with the histopathological criteria defined by the WHO. This case was not only a diagnostic challenge but also gives an idea of the cytological imprint of AOT. The histogenesis of AOT is unknown and thought to arise from odontogenic epithelium, remnant of dental lamina, Hertwig epithelial root sheath. Conservative surgical enucleation and curettage of the lesion are the treatment of choice. Recurrence of the tumor is very rare with an excellent prognosis.

**CONCLUSION**

Extra-follicular AOT of the maxilla is a rare occurrence posing a diagnostic challenge for clinician embodying clinico-radiological features is those mimicking with many odontogenic and inflammatory cysts. The final diagnosis of the AOT was made after histopathological examination although FNAC of the lesion in the given case has given a cytological inscription. AOT must be considered in the differential diagnosis of corticated radiolucency with or without small radiopaque foci, especially among young adults even in the absence of an impacted tooth.

**REFERENCES**

Choroidal Tuberculosis, Multiple Intracranial Tuberculomas and Spinal Cord Tuberculoma in a Patient with Choroidal Coloboma and Corectopia of Left Eye: A Case Report

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INTRODUCTION

The central nervous system (CNS) manifestation of tuberculosis (TB) is a rare but fatal without appropriate therapy. It accounts for 1% of TB cases with high morbidity and mortality across all age groups. Ocular disease is considered as a rare manifestation and has the wide prevalence across the patient populations and geography. It may be because of direct mycobacterial infection or hypersensitivity reaction. The most common forms of ocular TB include choroidal TB and tubercular uveitis. Early diagnosis and prompt treatment may be sight saving so screening for ocular involvement in every case of CNS TB. In comparison to ocular TB, spinal TB is a frequently observed extrapulmonary manifestation, in the form Pott’s spine, or can it exclusively involve spinal cord disseminated tuberculomas are a common in immunocompromised patient. We report an immunocompetent patient with no past h/o TB who presented with concurrent choroidal tubercles with multiple intracranial tuberculomas and intramedullary tuberculoma.

CASE REPORT

A 15-year-old boy visited our hospital with the chief complaints of fever of 10 days duration, weakness of both lower limbs for 4 days, double vision since 2 days, and headache and vomiting for 2 days before the hospitalization. A fever was low grade, intermittent associated with chills and the weakness of both lower limbs manifested in the form of inability to get up and walk was sudden in onset, non-progressive. He also had c/o blurring of vision and double vision on leftward gaze. The following day, he developed a headache associated with recurrent vomiting. On examination, he was a febrile with a regular pulse of 108/min, a supine blood pressure of 100/70 mmHg, a RR of 20/min, and SpO2 95% with room air. On the nervous system examination, he was conscious, oriented with normal higher mental functions and geography. It may be because of direct mycobacterial infection or hypersensitivity reaction. The most common forms of ocular TB include choroidal TB and tubercular uveitis. Early diagnosis and prompt treatment may be sight saving so screening for ocular involvement in every case of CNS TB. In comparison to ocular TB, spinal TB is a frequently observed extrapulmonary manifestation, in the form Pott’s spine, or can it exclusively involve spinal cord disseminated tuberculomas are a common in immunocompromised patient. We report an immunocompetent patient with no past h/o TB who presented with concurrent choroidal tubercles with multiple intracranial tuberculomas and intramedullary tuberculoma.
motor system examination, he had spastic paraparesis of both lower limbs with exaggerated reflexes. Upper limbs were normal and bilateral planters were extensor. Sensory system examination was essentially within normal limits with no cerebellar signs. On the basis of history and clinical examination, a possibility of meningitis was kept and in view of his paraparesis, raised ICT, headache and vomiting a possibility of an intracranial space occupying lesion was also considered. All his routine investigations including electrocardiogram and chest X-Ray were normal. His magnetic resonance imaging (MRI) brain revealed multiple ring-enhancing lesions distributed throughout the brain and screening through the spinal cord showed a single hypointense lesion in the cord opposite D5-D6 level.

In view of his abnormal pupil on the left side and c/o blurring of vision, we did a detailed ophthalmological examination which revealed the presence of an eccentric pupil (Corectopia) and choroidal coloboma of the left eye. Right eye showed the presence of choroidal tubercle along superotemporal quadrant with papilledema in both eyes. To rule out meningitis cerebrospinal fluid (CSF) was done, which showed a mild reduction of protein with normal cell count and glucose.

Our final diagnosis was multiple tuberculomas in brain, spinal cord, and choroid with congenital anomalies in the form of left eye choroidal coloboma and corectopia. He was started on anti-TB therapy daily regimen. He was improving during his course of hospitalization. His signs and symptom of intracranial tension were reduced. His left lateral rectus palsy improved over the period of 1-week. Power in lower limbs also improved and started walking. After the total hospital stay of 15 days at the time of discharge, he had no complaints of a headache and diplopia, his weakness in both lower limbs was recovered completely. A follow-up MRI is planned after a 1 month to look for resolution of tuberculomas in the brain, spinal cord as well as choroid (Figures 1-6).

**DISCUSSION**

Intracranial tuberculomas are a rare, the incidence is variably quoted between 2.3% and 18%. A major health hazard in developing countries usually involve cerebral and cerebellum due to rich blood supply and only 4% are located in brainstem. Our patient had tuberculomas in all these locations. CNS tuberculoma usually confused with intracranial neoplasm whenever present without signs and symptoms of TB. Depending on their size and location, intracranial tuberculomas can have many signs mimicking primary CNS tumors. Although intracranial tuberculomas generally exist as single lesions, 15-34% of them may be multiple. They have been found in all parts of the CNS and associated with focal neurological signs, seizure or increase in the intracranial pressure, they can also be asymptomatic. Miliary TB was found the most important independent factor linked to the development of ocular TB. Neuro-ophthalmic involvement, a part of its presentation spectrum, is important, and numerous reported neuro-ophthalmologic complications are combinations of oculomotor palsies, pupil abnormalities, disc changes suggestive of papillitis, papilledema, or optic atrophy and
Choroidal tuberculoma is the most common form of ocular TB and it is suggested that this is related to high blood supply of choroid. Only a few cases of choroidal tuberculomas have been reported and it has been considered uncommon (1%). However, Bouza et al. reported a high incidence of ocular TB (18%), and they suggested that these results might be related to the increase in the incidence of ocular TB and/or to detailed ocular examination of all TB patients.

Choroidal tuberculoma may present with or without active TB. Some cases with ocular TB may be asymptomatic and may be detected during routine ocular examinations. Choroidal and intracranial tuberculomas are formed by hematogenous spread from other active infected foci. Increasing the use of neuroimaging techniques has greatly helped in the early diagnosis of intracranial tuberculomas. It may be difficult to differentiate the MRI findings of tuberculomas from these lesions. Noncaseous tuberculomas usually have a hypointense signal on T1WI and a hyperintense signal on T2WI, with homogeneous enhancement after gadolinium administration. Solid caseous tuberculomas have iso-or hypo-intense signal on both T1WI and T2WI sequences. Diffusion-weighted MRI and magnetic resonance spectroscopy characteristics of TB lesions are neither sensitive nor specific. CSF analysis in intracranial tuberculomas without meningitis shows a mild lymphocytic pleocytosis with a nonspecific increase in protein content, and CSF bacteriology is usually negative.

Choroidal tuberculomas are frequently unilateral and appear predominantly in the posterior pole as solitary or multiple lesions. They are gray, grayish-white or yellowish and has indefinite borders. Although retinal vessels over lying these lesions appear normal, sometimes hemorrhage and/or exudation may be found. In the literature some authors reported late hyperfluorescence, others reported minimal early fluorescence with late staining by fundus fluorescein angiography (FFA). Since there are no typical FFA findings for choroid tuberculoma, FFA can contribute to exclusion of other causes. Histopathologic confirmation, which is needed for definite diagnosis of choroidal tuberculoma is not practical, therefore the diagnosis of choroidal tuberculoma is usually presumptive and is based on clinical and laboratory findings. Response to the treatment may be helpful to confirm the diagnosis of choroidal tuberculoma.

Our patient also had congenital ocular anomalies in the form of choroidal coloboma and corectopia of pupil which may be a chance detection and no reported association was found between these and tuberculomas.

CONCLUSION

Although CNS tuberculoma is a rare entity and usually presents with typical manifestation like headache, seizure, focal neurological deficit, and signs of raised intracranial...
pressure. It can present with atypical manifestation like diplopia and nystagmus as in our case. In developing countries where TB is endemic, CNS tuberculoma can present with atypical manifestations.

Since the delay in diagnosis and treatment results in poor prognosis and severe sequel, the effective therapy should be initiated as early as possible. In conclusion, early diagnosis, adequate treatment and follow-up for the response to the treatment of choroidal tuberculoma can prevent serious complications. Detailed ocular examinations should be performed in all cases with TB, for possible presence of early asymptomatic choroidal tuberculoma.

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Importance of Early Diagnosis of Hereditary Hemorrhagic Telangiectasia and Detection of Visceral Involvement Before Significant Clinical Complications Occur

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Abstract

Hereditary hemorrhagic telangiectasia is an autosomal dominant disorder that affects blood vessels throughout the body and results in a tendency for bleeding. The prognosis varies, depending on the severity of symptoms but generally, it is good when diagnosed early as bleeding is promptly recognized and adequately controlled. We report the case of a 45-year-old woman who developed telangiectasia over labial mucosa and ventral surface of the tongue, nasal septum, and multiple cherry angiomas over trunk was diagnosed as a case of hereditary hemorrhagic telangiectasia. She was successfully treated and prevented from developing further complications and followed up. Long-term systematic follow-up is indicated because known lesions may recur or progress and new manifestations of the syndrome may develop over time. Patients should be screened for pulmonary, hepatic, and central nervous system arteriovenous malformations (AVMs) at the time of diagnosis and at the onset of any suggestive symptoms and signs. Children of those with Hereditary hemorrhagic telangiectasia have a 50% chance of harboring the same mutation. Accordingly, pulmonary AVM screening and long-term follow-up are advocated.

Key words: Hereditary hemorrhagic telangiectasia (HHT), Arteriovenous malformations (AVMs), Recurrent epistaxis

INTRODUCTION

Hereditary hemorrhagic telangiectasia (HHT) manifested by mucocutaneous telangiectases and arteriovenous malformations (AVMs), a potential source of serious morbidity and mortality.¹ Lesions can affect the nasopharynx, central nervous system (CNS), lung, liver, and spleen as well as the urinary tract, urinary tract infections, conjunctiva, trunk, arms, and fingers.²³ Recurrent epistaxis is the most common presentation. ~90% manifest by the age of 40 years.¹ The reported case incidence is 1-2 cases per 1,00,000 populations annually. However, the prevalence may be underestimated because many cases may be asymptomatic. HHT occurs with equal frequency and severity in males and females.⁵

CASE REPORT

A 45-year-old female patient was admitted to Tirunelveli Medical College Hospital with complaints of hemoptysis 2 episodes, breathlessness for 2 months, and epistaxis on and off since 2 years. The patient had regular menstrual cycles with normal flow. The patient gave a history of multiple skin lesions present in her mother. There was no similar illness in any other family members. On general examination, telangiectasia was present over labial mucosa and ventral surface of the tongue (Figure 1) and nasal...
She had multiple cherry angiomas over trunk, which was blanching on pressure (Figure 2). She had pandigital clubbing. On auscultation, heart sounds were normal, and a bruit was heard over the right infrascapular area. Her vitals were stable, and other system examinations were normal. Her chest X-ray PA was normal. On further evaluating her, taking computed tomography (CT) chest revealed interesting findings (Figure 3) multiple lung nodules which were suggestive of AV malformation. So, we evaluated her by taking CT pulmonary angiography. Her CT pulmonary angiography (Figure 4) revealed multiple pulmonary AV malformations at least 12 with nidus of varying sizes in both lung fields supplied by segmental and subsegmental branches of pulmonary arteries and venous drainage through tributaries of pulmonary veins. Hence, we decided to take bubble echocardiogram which revealed small air bubbles in the left atrium.

**DISCUSSION**

Hereditary hemorrhagic telangiectasia is an autosomal dominant disorder manifested by mucocutaneous telangiectases and AVMs. Epistaxis is the most common manifestation. Onset of symptoms may be delayed until the fourth decade of life or later decades. Diagnosis of HHT is made clinically by the Curacao criteria:  
1. Epistaxis - Spontaneous, recurrent nosebleeds  
2. Telangiectases - Multiple at characteristic sites (lips, oral cavity, fingers, and nose)  
3. Visceral lesions - Gastrointestinal (GI) telangiectasia, pulmonary AVM, hepatic AVM, cerebral AVM, and spinal AVM  
4. Family history - A first-degree relative with HHT

Definite diagnosis - 3 criteria
Possible diagnosis - 2 criteria
Unlikely - <2 criteria

Skin lesions are managed by topical agents, hypertonic saline sclerotherapy, and Laser ablation. Pulmonary AVM is treated by embolization. GI bleeding is treated by aminocaproic acid and endoscopic photoablation or electrocautery. central nervous system AVM is treated by Embol therapy. Our patient gave the similar history in her mother, had episodes of epistaxis, had telangiectasia and her investigations revealed pulmonary AV malformations. Hence, she had all the criteria for definite diagnosis, and so our patient is a case of HHT.

CONCLUSION

This case illustrates the manifestations of HHT and its early diagnosis and management. Telangiectasia of skin and mucous membranes, epistaxis, and positive family history make up the classic triad of HHT. The onset of symptoms begins with epistaxis, continues with pulmonary AVMs, and proceeds to cutaneous and mucous telangiectases. Screening with multiple imaging modalities is employed in HHT because of the prevalence of AVMs. Medical therapy and surgical treatment in patients with HHT are aimed at decreasing the amount of hemorrhage and minimizing the sequelae of AVMs and that necessitates the early diagnosis of HHT.

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Endodontic Management of Taurodontism in Maxillary Molar: A Case Report

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Abstract

Taurodontism is a dental anomaly characterized by enlarged pulp chamber which may reach the proximity of root apex, apical displacement of the pulpal floor, and no constriction at the level of the cement-enamel junction. Despite the clinical challenges in endodontic therapy, taurodontism has received little attention from clinicians. In performing root canal treatment on such teeth, one should appreciate the complexity of the root canal system, canal obliteration and configuration, and the potential for additional root canal systems. This case report presents the taurodontism in tooth number 26 and 36. A conventional root canal treatment was carried out for these pulpally involved teeth.

Key words: Anomaly, Bull’s tooth, Enlarged pulp chamber, Taurodontism

INTRODUCTION

Taurodontism is an anomaly of tooth which is characterized by enlarged pulp chamber, apical displacement of the pulpal floor, and lacks of constriction at the level of the cement-enamel junction (CEJ).

This anomaly was first reported in the remnants of prehistoric hominids by De Terra in 1903 and by Gorjanovic, Kramberger, and Aldoff in 1907, and in 1909 Pickeril noted this in modern man. However, the term taurodontism (bull’s tooth) was first coined by Sir Arthur Keith in 1913.

The term taurodontism comes from “taoros” and “odontos,” meaning bull’s tooth (Keith, 1913; Terezhalmy et al., 2001), a condition that has been found in ancients Neanderthals where the teeth resemble that of cud chewing animals.

It is seen in both the permanent and deciduous dentition, unilaterally or bilaterally although permanent molar teeth are most commonly affected and infrequently in premolars also.³ While it appears most frequently as an isolated anomaly, its association with several syndromes such as hypophosphatasia or alteration of sex chromosomes such as Klinefelter’s syndrome, Trisomy 21, or Down’s syndrome.⁴

Incidence, as shown by an Israel study, was 5.6 %. It was reported to be lower than 1% in modern man, 3% in primitives, Eskimos, and American Indians.³ This retrograde or atavistic feature is because of its decrease in its incidence.

Despite the clinical challenges in endodontic therapy, taurodontism has received little attention from clinicians. In performing root canal treatment on such teeth, one should appreciate the complexity of the root canal system, canal obliteration and configuration, and the potential for additional root canal systems. Careful exploration of the grooves between all orifices particularly with magnification, use of ultrasonic irrigation, and a modified filling technique are of particular use.

Taurodontism in endodontic aspect presents challenge in non-surgical root canal therapy during negotiation, instrumentation, and obturation of the root canals.

This paper describes two case reports of the conventional endodontic treatment carried out with taurodontic teeth.
CASE REPORTS

Case 1
A 24-year-old male patient reported to the Department of Conservative Dentistry and Endodontics, YMT Dental College, Navi Mumbai, with pain in maxillary left posterior region since 2 weeks. On clinical examination, deep caries was seen with 26. The tooth was tender on percussion. Pre-operative radiographic examinations showed large pulp chamber and short roots, suggesting taurodontism. Periapical area was within normal limit (Figure 1a). The patient’s medical history and family history ruled out other diseases/pathologies occurring in association with taurodontism. Based on clinical and radiographic findings, diagnosis of irreversible pulpitis with acute apical periodontitis was made and endodontic therapy was planed for the same.

Under rubber dam and local infiltration of maxillary first molar, proper access opening made. The careful exploration revealed large pulp chamber, negotiation of the canals done, and it was found that three canals were originating deep into chamber. The working lengths were estimated using an apex locator (Propex, Dentsply) and then confirmed by radiograph (Figure 1b). After confirmation of three root canals mesiobuccal, distobuccal, and large palatal canal, the canals were prepared using a step back instrumentation technique up to 30# K file instruments for mesiobuccal and distobuccal canal and #40 for palatal canal at apex. A 2.5% of sodium hypochlorite and normal saline (sodium chloride injection I.P 0.9% w/v) was alternatively used as irrigants at every change of instruments. The canals were dried with sterile paper points and were dressed with calcium hydroxide paste. The access cavities were then temporarily sealed with intermediate restorative material. After an uneventful inter-appointment gap obturation of the root canals was undertaken by lateral condensation technique (Figure 1c). After obturation, the patient was followed up at regular intervals.

Case 2
A 35-year-old male patient reported to the Department of Conservative and Endodontics, YMT Dental College, Kharghar, Navi Mumbai, with chief complaint of pain in the lower left posterior region since 1 month. On clinical examination, large mesioproximal caries was seen with mandibular left third molar. Tooth was sensitive to percussion. The periapical radiograph showed large radiolucent periapical lesion at apex. Features of taurodontism were evident in intraoral periapical radiograph with mandibular left third molar. The patient's medical history and family history ruled out other diseases/pathologies occurring in association with taurodontism.

Under local anesthesia, access cavity preparation done, pulp extirpation done with all three canals before instrumentation. Both initial and final working length determined and confirmed with apex locator and radiograph. Instrumentation done with step back technique, mesiobuccal and mesiobuccal canals were prepared till #30 size K file and distal canal was prepared till #40 size K file. Normal saline and 2.5% sodium hypochlorite were used as an irrigation solution after each instrumentation. Calcium hydroxide closed dressing given for 1 week. The canals were obturated with 2% gutta percha using lateral condensation technique (Figure 2).

DISCUSSION

Taurodontism is an anomaly of multi-rooted teeth, characterized by enlargement of the pulp chamber. Widdowson defined taurodontism as the vertical deepening of pulp cavity at the expense of roots.6

Figure 1: (a) Pre-operative, (b) working length determination, (c) post obturation

Figure 2: (a) Pre-operative, (b) post-operative
In 1928, Shaw classified taurodontism into hypo, meso, and hyper taurodontism. In 1978, Shiffmann and Chanannel established more objective criteria on the basis of determined measurement of a tooth. A tooth is called taurodont when the distance from the lowest point of the pulp chamber roof (a) to the highest point of the floor (b) when divided by the distance from A to the root apex (c) should be equal to or >0.2 mm and/or the distance from B to cement CEJ (d) should be >2.5 mm.

The etiology of taurodontism is unclear. It is thought to be caused by the failure of Hertwig’s epithelial root sheath diaphragm to invaginate the proper horizontal level. Some reports suggest that taurodontism may be genetically transmitted (Fischer, 1963; Witkop, 1971; Goldstein and Gottlieb, 1973) and could be associated with an increased number of X chromosomes.

According to Mangion, taurodontism may be: A retrograde character, a primitive pattern, Mendelian recessive character, atavistic feature, a mutation.

While genetic transmission can be demonstrated in most cases, other external factors can also damage developing dental structures such as infection (osteomyelitis), disrupted developmental homeostasis, high-dose chemotherapy, and a history of bone marrow transplantation.

In taurodontism, the pulp chamber is extremely large and elongated with much greater apico-occlusal height than normal, and thus, extends apically below the CEJ. The CEJ constriction is less marked than that of the normal tooth, giving the taurodont a rectangular shape. Furthermore, the furcation is displaced apically, resulting in shorter roots while enlarging the body of the tooth.

Clinically, a taurodont appears as a normal tooth. In fact, because the body and roots of a taurodont tooth lie below the alveolar margin, its distinguishing features cannot be recognized clinically. Therefore, the diagnosis of taurodontism is usually a subjective determination made from diagnostic radiographs. The radiographic characteristics of taurodont tooth are: Extension of the rectangular pulp chamber into the elongated body of the tooth, shortened roots and root canals, location of furcation (near the root apices), despite a normal crown size.

Although permanent mandibular molars are most commonly affected, taurodontism can be seen in both the permanent and deciduous dentition (very low incidence), unilaterally or bilaterally, and in any combination of teeth or quadrants.

A taurodont tooth shows a wide variation in the size and shape of the pulp chamber, varying degrees of obliteration and canal configuration, apically positioned canal orifices and the potential for additional root canal systems. Therefore, root canal treatment becomes a challenge. Moreover, while the radiographic feature of a taurodont tooth is characteristic, pre-treatment radiographs produce little information about the root canal system. The results of pulp testing contribute little information about the effect of a large pulp chamber on tooth sensitivity.

Durr et al. suggested that morphology could hamper the location of the orifices, thus creating difficulty in instrumentation and filling. Each taurodont tooth may have extraordinary root canals in terms of shape and number. A complicated root canal treatment has been reported for a mandibular taurodont tooth with five canals, only three of which could be instrumented to the apex. Therefore, careful exploration of the grooves between all orifices, especially with magnification, has been recommended to reveal additional orifices and canals.

Because the pulp of a taurodont is usually voluminous, to ensure complete removal of the necrotic pulp, 2.5% sodium hypochlorite has been suggested initially as an irrigant to digest pulp tissue. Application of final ultrasonic irrigation may ensure that no pulp tissue remains.

Because of the complexity of the root canal anatomy and the proximity of the buccal orifices, complete filling of the root canal system in taurodontism is challenging. A modified filling technique has been proposed, which consists of combined lateral compaction in the apical region with vertical compaction of the elongated pulp chamber, using the system B device (EIE/Analytic Technology, San Diego, CA, USA).

In cases of hypertaurodont (where the pulp chamber nearly reaches the apex and then breaks up into two or four channels) vital pulpotomy; instead of routine pulpectomy may be considered as the treatment of choice.

Placement of post for tooth reconstruction in these large chambered teeth should be avoided.

CONCLUSION

Taurodont teeth show wide variations in the size and shape of pulp chambers, varying degrees of obliteration and canal complexity, lower level of canal orifices, and the potential for additional or extra root canal systems. It is very important for a general practitioner to be familiar of taurodontism and its complex root canal system, its clinical
significance, complication, and important endodontic consideration during its management.

Although endodontic management is very complex in taurodontic molars, this report describes the uneventful successful endodontic management of taurodontism in molar teeth with a promising prognosis.

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Clinical Spectrum of Granulomatosis with Polyangiitis-Wegener’s Granulomatosis: A Case Series

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Abstract
Granulomatosis with polyangiitis is a multi-organ system disease of unknown etiology, characterized by granulomatous inflammation, tissue necrosis, and variable degrees of vasculitis in small- and medium-sized blood vessels. It is rare and commonly missed. Here, we present three cases who have been followed for 1-3 years.

Key words: Granulomatous inflammation, Necrotizing vasculitis, Polyangiitis-Wegener’s

INTRODUCTION

Granulomatosis with polyangiitis is a granulomatous necrotizing vasculitis characterized by a predilection to affect the upper and lower respiratory tracts and, in most cases, kidneys.¹ The disease was first described in 1931 by Heinz Klinger, a German medical student.²³ In 1936 and 1939, Friedrich Wegener, a pathologist, provided detailed information about three patients with a similar illness. It has been subsequently redesignated as granulomatosis with polyangiitis.² It is classified as anti-neutrophil cytoplasmic antibodies (ANCA) positive vasculitis mostly localized on the small and medium- sized blood vessel.¹⁶ Although distinctive patterns of organ involvement exist in Granulomatosis with polyangiitis, any organ system can become affected.¹⁷

It has a predilection for causing destructive lesions in the upper respiratory tract, including nasal septal perforation, “saddle-nose” deformity, erosive sinusitis, middle ear damage, and subglottic stenosis.⁸⁹ Classic lung lesions are pulmonary nodules with a tendency to cavitation, alveolar hemorrhage and non-specific infiltrates.¹⁰¹¹ Glomerulonephritis that leads to crescentic and segmental, necrotizing lesions, is often associated with rapidly progressive glomerulonephritis.¹²¹³ Migratory oligoarthralgias and oligoarthritis are common.¹⁸ Granulomatosis with polyangiitis cases, particularly those with severe, widespread disease, are associated with anti-neutrophil cytoplasmic antibodies.⁶¹¹ The sensitivity of proteinase 3 (PR3-ANCA) is about 90% in active WG and 40% when the disease is in remission. The specificity of PR3-ANCA in the diagnosis of WG exceeds 95%.¹⁴¹⁵¹²¹⁶ For patients with limited WG, defined as the absence of an immediate threat to either the function of a vital organ or the patient’s life, 30% or more lack ANCA.¹⁶⁻¹⁸ Immunosuppressive therapy is effective in the induction of disease remissions in most cases. Untreated systemic WG had a dismal prognosis, with a mean survival of approximately 5 months.¹²¹⁹ Not much data is available on the epidemiology of WG in India. A study conducted at AIIMS, New Delhi detailed 23 cases of WG between 1988 and 2000. 16 of the patients were male and 7 were female.²⁰ In another study conducted at KEM Mumbai 25 patients of WG were diagnosed over a period of 4 years. There were 23 cases where generalized WG two cases of limited WG.²¹

Here, we present a case series comprising of three cases which reflects the wide spectrum of clinical presentation of this disease.
CASE SERIES

Case 1
A 43-year-old female presented with 4 months history of fever, polyarthritis, purulent ear discharge, hemoptysis, parotitis, scleritis of left eye, and decreased urination. Patient was treated for chronic sinusitis, and otitis media elsewhere but the condition did not improve. On the day of admission the patient was conscious afebrile, her pulse was regular 86/min, BP was 130/86 mm of Hg. She had severe pallor, nodular scleritis of left eye, non-foul smelling discharge from right ear, and symmetrical polyarthritis. Audiometry revealed B/L sensorineural deafness. Examination of cardiovascular and respiratory system was normal. Gastrointestinal (GI) system and central nervous system (CNS) were normal. On the 4th day of admission, patient developed anuria and received hemodialysis. She developed hypertension during the course of her stay in the hospital which was controlled by calcium channel blockers and diuretics.

X-ray of chest was normal. Computed tomography (CT) thorax showed multiple nodules in left upper and right lower lobes, diffuse ground glass opacity, with sepal thickening in B/L perihilar region. Cavity was present in left upper lobe along with B/L pleural effusion. All these findings were suggestive of WG. USG abdomen and pelvis revealed B/L acute medical renal disease along with moderate ascites.

A diagnosis of generalized granulomatosis with polyangitis was made based on involvement of lungs, upper respiratory tracts, kidneys, positive ANCA, and anti-PR-3 antibody (>200 Ru/ml) (Table 1).

Following the confirmation of diagnosis patient was given 1 g methyl prednisolone bolus daily for three days followed by tab prednisolone 1 mg/kg body weight. She was also started on tab cyclophosphamide 2 mg/kg, with a starting dose of 50 mg/day. It was increased to 75 mg/day with dose modification based on her serum creatinine levels. She received four sessions of hemodialysis and was given four units of blood transfusion. Patient was discharged with cyclophosphamide 75 mg/day, prednisolone 50 mg/day, anti-hypertensives, and calcium supplements. At the time of her discharge her hemoglobin (HB) was 8 g%. Renal function had improved. Her serum creatinine was 2.6 mg/dl and serum urea was 86 mg/dl. She requested to be discharged was asked to report after 1 months but failed to return.

8 months later she was readmitted with complaints of generalized weakness and swelling of feet. Her HB was 6.5 g%, serum creatinine was 4.6 mg/dl, serum urea was 126 mg/dl. Her thin layer chromatography 9800/cmm, DC-N-86% L-11% E-2% L-1%, Random blood sugar (RBS) 100 mg/dl. Liver function was within normal limits. Urine contained traces of albumin, plenty of red blood cells, 20-30 pus cells/HPF, there was no scleritis, ear discharge, polyarthritis, or fever. Her X-Ray showed no lesions. She was given 3 bolus doses of methylprednisolone of 1 g each along with mycophenolate mofetil, 1 g/day and advised to increase the dose to 2 g over 2 weeks period since she was unable to afford Rituximab for financial reason.

She had already received 13 g of oral cyclophosphamide and therefore mycophenolate was preferred to avoid toxicity in the background of deteriorating renal function renal function. The patient requested a discharge and was asked to follow up a month later. However, the patient never returned.

Case 2
A 48-year-old male presented with 4 years history of chronic sinusitis, and polyarthralgia. He gave history of epistaxis and nasal discharge for which he was treated by the ENT specialist. A nasal growth was observed for which he underwent a biopsy. Histopathological examination showed evidence of chronic inflammation. Subsequently, he was admitted in the unit of clinical immunology for prolonged cough, fever and hoarseness of voice. On examination patient was afebrile, pulse rate 84/min BP 116/70 mmHg examination of the lungs revealed basal crepitation. Examination of upper respiratory tract revealed maxillary sinusitis. He had a saddle shaped nose, congested, and swollen vocal chords were found in the laryngoscopic

### Table 1: Investigations of case 1

<table>
<thead>
<tr>
<th>Investigation</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>TLC</td>
<td>23180/cm²</td>
</tr>
<tr>
<td>DC</td>
<td>N 90% L 9% E 1%</td>
</tr>
<tr>
<td>HB</td>
<td>4.3 g/dl</td>
</tr>
<tr>
<td>TPC</td>
<td>5,20,000</td>
</tr>
<tr>
<td>ESR</td>
<td>155</td>
</tr>
<tr>
<td>Serum urea</td>
<td>63</td>
</tr>
<tr>
<td>Serum creatinine</td>
<td>5.9</td>
</tr>
<tr>
<td>S. Na</td>
<td>125</td>
</tr>
<tr>
<td>S. K</td>
<td>5.9</td>
</tr>
<tr>
<td>Serum bilirubin (T)</td>
<td>1.2</td>
</tr>
<tr>
<td>Serum bilirubin (D)</td>
<td>0.4</td>
</tr>
<tr>
<td>SGPT</td>
<td>48</td>
</tr>
<tr>
<td>SGOT</td>
<td>48</td>
</tr>
<tr>
<td>ALP</td>
<td>185</td>
</tr>
<tr>
<td>Urine pus cells</td>
<td>15-20/HPF</td>
</tr>
<tr>
<td>Urine RBC</td>
<td>&gt;100/HPF</td>
</tr>
<tr>
<td>Urine albumin</td>
<td>Trace</td>
</tr>
<tr>
<td>Urine sugar</td>
<td>Absent</td>
</tr>
<tr>
<td>C-ANCA</td>
<td>Positive</td>
</tr>
<tr>
<td>Anti PR-3</td>
<td>&gt;200 Ru/ml</td>
</tr>
<tr>
<td>(0-20) Ru/ml</td>
<td></td>
</tr>
</tbody>
</table>

TLC: Thin layer chromatography, RBS: Random blood sugar, HB: Hemoglobin, Anti PR-3: Anti proteinase 3
Nath, et al.: Granulomatosis with Polyangiitis-Wegener’s Granulomatosis

30 mg/dl
105
0.9 mg/dl
14.4 g%
1.0 mg/dl
18,600 N 89%, L10% E 1%
28.9 (N≤9)
27 mg/dl
100 mg/dl
N85, L 11, E4
12.6
20,600
38
48
116
28.9 (N=59)
NEGATIVE
0.4 mg/dl
40 mg/dl
1.3 mg/dl
48

Case 3

Our third case was 54-year-old women who presented with 6 years history of chronic sinusitis, headache, hoarseness of voice and non-productive cough. There was no history of hypertension or type 2 DM. On examination the patient was febrile. Her pulse was 100/min, BP was 136/70. She had tender sinusitis left sided lid edema, palpable purpurae on lower limb suggestive of cutaneous vasculitis. ENT examination revealed laryngeal edema. Abdomen was soft and non-tender. CVS and CNS examination was normal. X-Ray paranasal sinuses (PNS) revealed pansinusitis, X-Ray chest was normal. High resolution CT thorax showed lower lobe infiltrations, CT scan of PNS showed several maxillary sinusitis. Her C-ANCA was negative and anti-PR-3 was negative. She was diagnosed as case of limited form of granulomatosis with polyangiitis based on the involvement of upper respiratory tracts, lungs, and cutaneous vasculitis. She was started on antibiotics for sinusitis, and prednisolone 1 mg/kg body weight.

A drainage of PNS was planned but deferred. When the patient was readmitted for PNS drainage, routine investigation revealed RBS of 300 mg/dl. Her HBA1C was 8.1, FBS was 286 and PPBS was 312. She also had lobar pneumonia. Patient was started on regular insulin and broad spectrum antibiotics.

Subsequent biopsy of PNS showed evidence of chronic inflammation. She was discharged after the infection subsided and blood sugar was stabilized. She was on maintenance dose of prednisone (7.5 mg/day) methotrexate (10 mg/day) and cotrimoxazole prophylaxis. After 1 year, the patient has remained relatively asymptomatic (Table 3 and Figures 1-3).

DISCUSSION

Granulomatosis with polyangiitis (Wegener’s) is an uncommon disease with an estimated prevalence of 3/100,000.22 It is extremely rare in blacks compared with whites; the male-to-female ratio is 1:1.22 The disease can be seen at any age; 15% of patients are <19 years of age, but only rarely does the disease occur before adolescence; the mean age of onset is 40 years.22 Involvement of the upper airways occurs in 95% of patients with granulomatosis with polyangiitis (Wegener's).23 Patients often present with severe upper respiratory tract findings such as paranasal sinus pain and drainage and purulent or bloody nasal discharge, with or without nasal mucosal ulceration.8,10,11 Nasal septal

<table>
<thead>
<tr>
<th>Table 2: Laboratory investigations of case 2</th>
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</thead>
<tbody>
<tr>
<td><strong>Parameter</strong></td>
</tr>
<tr>
<td>TLC, ESR</td>
</tr>
<tr>
<td>DC</td>
</tr>
<tr>
<td>RBS</td>
</tr>
<tr>
<td>Serum urea, serum creatinine</td>
</tr>
<tr>
<td>Serum bilirubin T Serum bilirubin D</td>
</tr>
<tr>
<td>SGOT</td>
</tr>
<tr>
<td>SGPT</td>
</tr>
<tr>
<td>ALP</td>
</tr>
<tr>
<td>Anti MPO</td>
</tr>
<tr>
<td>ANCA, Anti PR3</td>
</tr>
<tr>
<td><strong>Note:</strong> Anti PR3, TLC: Thin layer chromatography, RBS: Random blood sugar, ANCA: Anti-neutrophil cytoplasmic antibodies, HB: Hemoglobin</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Table 3: Laboratory investigations of case 3</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Parameter</strong></td>
</tr>
<tr>
<td>TLC, DC</td>
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<tr>
<td>TPC</td>
</tr>
<tr>
<td>ESR</td>
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<tr>
<td>Serum urea</td>
</tr>
<tr>
<td>Serum creatinine</td>
</tr>
<tr>
<td>Bilirubin (t)</td>
</tr>
<tr>
<td>Bilirubin (d)</td>
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<tr>
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<tr>
<td>ALP</td>
</tr>
<tr>
<td>RBS</td>
</tr>
<tr>
<td>CRP</td>
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</tbody>
</table>

**Note:** PR3: Proteinase 3, TLC: Thin layer chromatography, RBS: Random blood sugar, ANCA: Anti-neutrophil cytoplasmic antibodies, HB: Hemoglobin
perforation may follow, leading to saddle nose deformity. Serous otitis media may occur as a result of Eustachian tube blockage. Subglottic tracheal stenosis resulting from active disease or scarring occurs in 16% of patients and may result in severe airway obstruction. Pulmonary involvement may be manifested as asymptomatic infiltrates or may be clinically expressed as cough, hemoptysis, dyspnea, and chest discomfort. It is present in 85-90% of patients. Eye involvement (52% of patients) may range from a mild conjunctivitis to dacryocystitis, episcleritis, scleritis, granulomatous sclerouveitis, and ciliary vessel vasculitis. Renal disease (77% of patients) generally dominates the clinical picture and, if left untreated, accounts directly or indirectly for most of the mortality. Cutaneous manifestations have been reported in 40-50% of patients with WG and may be part of the initial presentation in 13-25% of cases. The cutaneous manifestations of WG include ulcers, palpable purpura, subcutaneous nodules, papules, and vesicles. Prior to the introduction of effective therapy, granulomatosis with polyangiitis (Wegener’s) was universally fatal within a few months of diagnosis.

In 1990, the American College of Rheumatology (ACR) established the criteria for the classification of WG as nasal or oral inflammation, radiologically demonstrated pulmonary infiltrates, abnormal urinary sediment (red cell cast, hematuria), granulomatous inflammation on biopsy. Patients are diagnosed with Wegener’s granulomatosis if 2 of these 4 criteria are present. The presence of autoantibodies to proteinase 3/cANCA is not required for diagnosis of WG, by either ACR or Chapel Hill consensus Conference definition.

Glucocorticoids alone led to some symptomatic improvement, with little effect on the ultimate course of disease. The development of treatment with cyclophosphamide dramatically changed patient outcome such that marked improvement was seen in >90% of patients, complete remission in 75% of patients, and 5-year patient survival was seen in over 80%. After 3-6 months of induction treatment, cyclophosphamide should be stopped and switched to another agent for remission. The agents with which there has been the greatest published experience are methotrexate and azathioprine. In the absence of toxicity, maintenance therapy is usually given for a minimum of 2 years past remission, after which time consideration can be given for tapering over a 6-12 month period until discontinuation.

In two recent randomized trials that enrolled ANCA positive patients with severe active granulomatosis with polyangiitis (Wegener’s) or microscopic polyangiitis, rituximab 375 mg/m² once a week for 4 weeks in combination with glucocorticoids was found to be as effective as cyclophosphamide with glucocorticoids for inducing disease remission.

In our case report, we have shown the wide spectrum of clinical presentation of the disease. Two of the patients were female and one was male. The mean age at
presentation was 48 years. All the three case had upper respiratory tract involvement in the form of chronic sinusitis. One of our patients had sensorineural hearing loss. Cutaneous vasculitis and saddle nose deformity were also found. Lung involvement was present in all three of the patients. All three of them showed different forms of lung involvement each of which has been described in WG. Our first case is the classical case of granulomatosis with polyangiitis. In the second case, the spectrum gradually changed from limited granulomatosis with polyangiitis to classical variety. The third case has remained in limited form. In our set up the main drawback is late presentation with delayed diagnosis. All these patients were treated for chronic sinusitis and were given Non-steroidal anti-inflammatory drug (NSAIDS)/antibiotics in view of the high leukocyte count. NSAID may precipitate renal failure or aggravate an already dysfunctional kidney.

CONCLUSION

Granulomatosis with polyangiitis has wide spectrum clinical manifestations. It should always be considered as differential diagnosis in patients with intractable sinusitis, deafness and oitis media. Since renal involvement at times can be subtle utmost caution should be exercised while prescribing NSAIDS to these patients.

REFERENCES


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