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# Conduction Blocks in Acute Myocardial Infarction: A Prospective Study

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## Abstract

**Introduction:** Coronary artery disease is a worldwide disease. Ischemic heart disease is the cause of 25-30% of deaths in most industrialized countries. Electrocardiogram is the most useful and feasible diagnostic tool for the initial evaluation, early risk stratification triage, and guidance of therapy in patients who have chest pain.

**Materials and Methods:** This is a prospective hospital-based study, comprising of 232 patients diagnosed with acute ST-elevation myocardial infarction (STEMI) admitted to ICCU in the Mahatma Gandhi Memorial (MGM) Hospital, Warangal, who developed conduction disturbances.

**Results:** This is a prospective hospital-based study, comprising of 232 patients diagnosed with acute STEMI admitted to the ICCU in MGM Hospital, Warangal, who presented from November 2012 to October 2013. Out of them, 36 (15.5%) patients were noted to have conduction blocks.

**Conclusion:** Developing heart block is an indirect measure of the severity and extension of the disease in patients with acute myocardial infarction.

**Key words:** Acute Myocardial Infarction, Blocks, Conduction

## INTRODUCTION

Coronary artery disease (CAD) is a worldwide disease. Ischemic heart disease is the cause of 25-30% of deaths in most industrialized countries.

Electrocardiogram (ECG) is the most useful and feasible diagnostic tool for the initial evaluation, early risk stratification triage, and guidance of therapy in patients who have chest pain. Patients with ST elevation or new left bundle branch block (LBBB) are considered to have acute myocardial infarction (AMI) and are usually referred for immediate reperfusion therapy, whereas those without ST elevation or those with predominantly ST depression are usually treated conservatively initially.

Bradyarrhythmias and conduction blocks (CB) are well-recognized complications of AMI. They are induced by either autonomic imbalance or ischemia and necrosis of the conduction system. It is important to recognize that bradyarrhythmias are transient and that are likely to progress to irreversible and symptomatic high-degree block. ECG reflects the physiology of the myocardium during acute ischemia. Various types of CB develop following AMI. First-degree atrioventricular block (AVB) occurs in 4-14% of patients with AMI; Mobitz Type I second-degree AVB is observed in up to 10% of patients with AMI and is usually transient. Mobitz Type II second-degree AVB occurs in >1% of patients with AMI.<sup>1</sup> Third-degree or complete AVB occurs in about 5-8% of patients.<sup>2</sup> The development of BBB, complete AVB is associated with poor prognosis likely owing to the extensive nature of the infarction.<sup>1</sup>

Defining the incidence and prognostic significance of new conduction abnormalities associated with AMI is complicated for several reasons. Data are most commonly generated from retrospective reviews or sub-analyses of clinical trial data. Much of the data on bradyarrhythmias and BBB predate the development of primary reperfusion

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therapies (thrombolysis and primary percutaneous coronary intervention). By reducing infarct size, these therapies may also reduce the incidence of new conduction abnormalities, although the prognostic significance of new conduction abnormalities, when they occur, may be similar.<sup>3</sup>

The presence or absence of BBB is usually determined on the initial ECG. Uncertainty regarding the age of BBB also impacts the interpretation of prognostic data. Chronic and new conduction abnormalities may both predict poorer outcomes but for different reasons: The former due to more extensive underlying cardiac disease and the latter due to the association with larger infarctions.

In the present day scenario, especially in our subset of patients, the risk factor profiles have changed. Furthermore, the age of onset of CAD has decreased with more number of patients having diffuse disease including multivessel disease (interheart study).

Furthermore, no study has been done in our subset of patients on CB and their prognostic implications. The present study is aimed at observing patterns of various CB and their prognostic implications in AMI.

## MATERIALS AND METHODS

This is a prospective hospital-based study, comprising of 232 patients diagnosed with acute STEMI admitted to the ICCU in Mahatma Gandhi Memorial (MGM) Hospital, Warangal, who developed conduction disturbances.

### Place of Study

ICCU, MGM Hospital, Warangal, Telangana, India.

### Study Population

Conduction abnormalities in Patients presenting with AMI.

### Period of Study

The study period is from November 2012 to October 2013.

Before the commencement of the study, permission was obtained from the department with an approval of the protocol of the study. All enrolled patients were informed about the nature of the study and their rights to refuse. Their written consent was taken before including them in the study.

A detailed history was taken about the chest pain, the presence of risk factors and duration of risk factors as appropriate. A detailed history was also obtained about the use of different medications. Random venous blood sample was obtained for analysis of blood glucose, lipid profile, renal function test, and routine blood investigations.

A diagnosis of AMI was made on the basis of chest pain lasting >30 min; ST-segment elevation  $\geq 1$  mm in at least two of the limb leads and elevation of creatine kinase enzyme and its myocardial band (MB) fraction to more than twice the upper limit of normal or troponins.

Following admission into ICCU, all the patients were followed up, and special attention was paid to detect the occurrence of CB. Continuous electrocardiographic monitoring was performed for an average of 48 h. Standard 12-lead ECG was taken on admission into ICCU, at a paper speed of 25 mm/s and an amplification of 10 mm/mV.

In an acute phase, the repeat ECG was recorded whenever the clinical condition required and every 12 h thereafter for the first 2 days and then once daily and more frequently if a change in rhythm or conduction was noted. The isoelectric line defined as the level of the preceding TP segment. The degree of ST segment elevation and depression was measured to the nearest 0.5 mm at the J-point in each of the 12 standard leads.

ECG criteria for the diagnosis of STEMI: New ST elevation at J-point in two contiguous leads with cut points:  $\geq 0.1$  mv in all leads other than leads V2-V3 where the following cut points apply:  $\geq 0.2$  mv in men  $\geq 40$  years,  $\geq 0.25$  mv in men < 40 years,  $\geq 0.15$  mv in women.

The diagnosis of various CB was made based on the following ECG features:

- First-degree AVB: PR interval of more than 0.20 s
- Second-degree AVB: Intermittent failure of AV conduction.
  - Mobitz Type I: Characterized by Wenckebach cycle, beginning with normal or prolonged PR interval and, with each successive beat, the PR interval lengthens until the block of the supraventricular impulse occurs and a beat is dropped. The pause is shorter than the PR interval of any two consecutively conducted beats. The shortest PR interval follows and the longest PR interval precedes the ventricular pause.<sup>4,5</sup>
  - Mobitz Type II: There is an intermittent failure of AV conduction, but the PR intervals of all the conducted supraventricular impulses are constant.
- Third-degree or complete AVB:<sup>4</sup> It is characterized by:
  1. AV dissociation: "P" waves bear no relationship to QRS complexes.
  2. Slow ventricular rate: Usually in the range of 30-35 bpm if subsidiary pacemaker is situated in ventricles and in the range of 35-40 bpm if subsidiary pacemaker is situated in the lower AV node (i.e., below the block) or in the bundle of His.

3. QRS configuration: If subsidiary pacemaker is situated in the lower AV node (i.e., below the block) or in the bundle of His, QRS configuration is normal or near normal and it is abnormal, being broad, notched, slurred, and bizarre if the pacemaker is situated in the ventricular musculature.
- Left anterior hemiblock (LAHB)<sup>5-7</sup>
  - Frontal plane mean QRS axis of  $-45^{\circ}$  to  $-90^{\circ}$
  - QRS duration less than 120 ms
  - qR pattern in leads I and aVL
  - Late intrinsicoid deflection in aVL ( $>0.45$  s)
  - RS pattern in leads II, III, and aVF.
- Left posterior hemiblock (LPHB)<sup>5-7</sup>
  - Frontal plane mean QRS of  $\geq +120^{\circ}$
  - QRS duration of  $<120$  ms
  - Small initial “r” wave and prominent “S” wave in leads I and aVL
  - qR pattern in leads II, III, and aVF
  - Late intrinsicoid deflection in aVF ( $>0.045$  s)
  - Exclusion of other causes of right axis deviation.
- LBBB

#### Features of complete LBBB:<sup>5</sup>

- QRS duration  $\geq 120$  ms
- Broad, notched “R” waves in lateral precordial leads (V5 and V6) and usually in leads I and aVL
- Absent septal “q” waves in left-sided leads
- Small or absent initial “r” waves in right precordial leads (VI and V2) followed by deep “S” waves
- Prolonged intrinsicoid deflection ( $>60$  ms) in V5 and V6.

#### Features of incomplete LBBB:<sup>5</sup>

- Loss of septal “q” waves
- Slurring and notching of the upstroke of “R” waves
- Modest prolongation of the QRS complex (between 100 and 120 ms)
- Right bundle branch block (RBBB).

#### Features of complete RBBB:<sup>5</sup>

- QRS duration  $\geq 120$  ms
- Broad, notched “R” waves (“rsr,” “rsR,” or “rSR” pattern) in right precordial leads (VI and V2)
- Wide and deep “S” waves in left precordial leads (V5 and V6).

#### Incomplete RBBB:<sup>5</sup>

- “RSr” pattern in lead V1 with a QRS duration between 100 and 120 ms.

#### RBBB plus LAHB:<sup>5</sup>

- Characterized by ECG pattern of RBBB plus left axis deviation beyond  $-45^{\circ}$ .

#### RBBB plus LPHB:<sup>5</sup>

- Characterized by ECG pattern of RBBB plus a mean QRS axis deviation to the right of  $+120^{\circ}$ .

#### Cardiac enzymes:

- CPK-MB
- Troponin I-positive/negative
- The biochemistry tests were done in MGM Hospital, Warangal.

#### Statistical Analysis

1. Continuous variables are presented as mean  $\pm$  standard deviation and frequency variables as percentages
2. Chi-square and Fisher's exact test were performed for statistical significance.  $P < 0.05$  was considered for statistical significance
3. SPSS software version 20.0 was used for statistical analysis.

#### Inclusion Criteria

Patients having AMI as per the WHO criteria<sup>8</sup> that is at least two of the following three elements be present:

1. History of ischemic type of chest discomfort
2. Evolutionary changes on serially obtained electrocardiograph tracings
3. A rise and fall in serum cardiac markers.

#### Exclusion Criteria

1. Patients with previous CB
2. Patients with cardiomyopathy
3. Patients with congenital or rheumatic heart disease
4. Patients with history of intake of drugs causing CB such as clonidine, methyldopa, verapamil, and digoxin.

## RESULTS

This is a prospective hospital-based study, comprising of 232 patients diagnosed with acute STEMI admitted to the ICCU in MGM Hospital, Warangal, who presented from November 2012 to October 2013. Out Of them, 36 (15.5%) patients were noted to have CB.

The age of the study group ranged from 25 to 90 years ( $54.78 \pm 13.27$ ). The majority of the patients belonged to age group of 50-69 years (51.28%). Among male patients, majority belonged to the age group 50-59 years, compared to the females majority of whom were in the age group of 60-69 years.

Smoking was the most common risk factor in males (53.1%), followed by hypertension and diabetes. In female patients, hypertension and diabetes were the commonest risk factors (52.5%).

Smoking is the most common risk factor seen in 79 (40.3%) patients without blocks and 12 (33.3%) patients with blocks followed by hypertension in 62 (31.6%) without blocks and 10 (27.7%) patients with blocks. Diabetics had a significantly higher rate of occurrence of CB. No much difference was noted between the two groups overall.

Chest pain was the most common symptom overall and was noted in 193 (98.4%) patients without blocks and 29 (80.5%) patients with blocks. Breathlessness, palpitations, vomitings, and giddiness were more common in patients with CB compared to those without CB, and this was statistically significant.

Bradycardia, hypotension, and raised JVP are more common in patients with CB as compared to patients without CB.

Anterior or lateral wall AMI accounted for 56.8% of all cases, whereas inferior or posterior wall accounted for 43.2% of all cases. First-degree heart block was the most common of all (25%), followed next by LBBB (19.4%). BBB accounted for 69.4% of all conduction abnormalities noted. The incidence of CB was higher among patients with anterior or lateral wall AMI than the posterior or inferior wall AMI which was statistically insignificant ( $P = 0.35$ ). 72.7% of AVB occurred in inferior wall AMI, whereas 76% of bundle branch blocks occurred in anterior wall AMI, which was statistically significant ( $P = 0.04$ ).

Cardiogenic shock was the most common complication noted, seen in 17.2% of all cases. All cases with third-degree heart block and RBBB eventually died mean heart rate, systolic and diastolic blood pressures were lower in patients who had CB. In addition, CB occurred in slightly higher age group of patients.

About 33.3% and 10.2% of patients with and without CB, respectively, died, projecting the higher mortality associated with the development of CB. Elderly patients, diabetics, who are not thrombolysed were associated with the development of CB significantly. Similarly, CB were associated with higher risk of development of acute kidney injury and outcome death.

Advanced age, occurrence of inferior or posterior wall AMI, failure to receive thrombolytic therapy, and development of acute kidney injury during hospital stay are found as independent predictors of in-hospital mortality in my study.

## DISCUSSION

232 patients of AMI were selected from cases admitted in ICCU, MGM Hospital, Warangal from November 2012 to

October 2013. Out of 232 cases taken into the study 36, (15.5%) patients were noted to have CB.

### Age

In the present study, the mean age of study population was 54.78 years. The subgroup with CB had a mean age of 55.55 years and the subgroup without CB had a mean age 54.34 years. The patients with CB were slightly elder than those without CB; it was statistically significant. Eriksson *et al.* reported the similar finding, as did other studies. One recent study by Shirafkan *et al.*<sup>9</sup> failed to show any correlation between age and incidence of CB. This could be attributed to the difference in demographic profile as well as racial, genetical disparities and also changing patterns of the population at risk.

Various registries across the world showed the mean ages of the person developing STEMI to be around 63-69 years. In another recent study from India (Create Registry<sup>10</sup>), the mean age was 57 years. Another similar study done by Shirafkan *et al.*<sup>9</sup> had a mean age group of 65.8 years.

On comparison with other studies, patients in our study were younger, corroborating with the emerging evidence from various recent studies, that CAD occurs a decade earlier in Indian population.<sup>11</sup> This also emphasizes the growing prevalence of CAD as well as a change of the population at risk.

### Sex

In the present study group, 68.9% were males and 31.1% were females with male to female ratio of 2.2:1. Our figures are not very much different in comparison with study done by Newby *et al.* and Shirafkan *et al.*<sup>9</sup>

In various other studies the reported M: F ratio varied from 3.6:1 (Vakil, 1962) to 2.4:1 (Singh *et al.*, 1977).<sup>12</sup> The decreasing sex ratio when compared to the older studies could be due to the increasing incidence and prevalence of CAD in Indian females.

Among males, majority belonged to the age group 50-59 years, compared to the females, majority of whom were in the age group of 60-69 years. Mean age of presentation in females was more than in males (60.9 vs. 52.07 years).

### Risk Factors

Smoking was the most common risk factor in males (53.1%), followed by hypertension and Diabetes. In female patients, hypertension and diabetes were the commonest risk factors (52.5%). Apart from smoking, other risk factors were not much different between male and females. In the present study, smoking was the most common risk factor in cases with and without blocks, followed by hypertension and diabetes.

Of 232 patients in the study, 132 (56.9%) had features suggestive of anterior wall AMI and 100 (43.1%) had inferior wall AMI. This was nearly similar to the previous studies reported. In a study by Shirafkan *et al.*,<sup>9</sup> of 400 patients, 255 (63.75%) showed electrocardiographic and echocardiographic evidence of anterior AMI, whereas 145 (36.5%) had inferior AMI.

Most of AVBs (72.7%) were seen in inferior/posterior wall AMI, whereas 76% of intraventricular blocks were associated with anterior/lateral wall AMI. These results were concurrent with the study done by Majumdar *et al.*,<sup>13</sup> which are 92% and 72%, respectively. In a study by Shirafkan *et al.*,<sup>9</sup> 79.5% of the blocks in patients with anterior AMI were of intraventricular type, whereas 68.4% of the blocks which happened after inferior AMI were AV type blocks.

The first-degree AVB was the most common as well as the most common AVB noted in the present study accounting for 25% of the total conduction defects. Third-degree AVB (complete heart block [CHB]) was seen in 5.5% which was near similar to that of study by Shirafkan *et al.*<sup>9</sup> (4.8%).

Another study by Nguyen *et al.*<sup>14</sup> found that the overall proportion of patients with AMI who develop CHB is 4.1% and emphasized that the incidence of CHB complicating AMI has declined appreciably over time, with the greatest decline in these incidence rates occurring during the most recent years (2.0% of patients hospitalized with AMI in 2005 vs. 5.1% in 1975).

LBBB was the most frequent type of intraventricular block, unlike the study by Shirafkan *et al.*<sup>9</sup> where LAHB was the most common. This was followed by LAHB which accounted for 16.6% of the total blocks. In a study by Shirafkan *et al.*,<sup>9</sup> LAHB was the most common followed by LBBB and RBBB which accounted for 30.2%, 19%, and 9.5% of the cases, respectively. Elizari *et al.*<sup>15</sup> also noted the presence of a frequent association between anteroseptal myocardial infarction and LAHB.

LPHFB was the least common similar to the earlier studies. As stated by Basualdo *et al.*,<sup>16</sup> the posterior division of the left bundle is relatively short and thick and hence is less exposed to mechanical trauma than its anterior counterpart. In addition, the posterior division of the left bundle probably receives a double blood supply from both the left anterior descending and the right coronary arteries. These anatomical considerations explain the fact that LPHB is an infrequent complication of AMI and that it is commonly associated with other conduction disturbances.

The reasons for the differences from the previous studies could be probably explained by the demographic, regional,

and cultural variations between the earlier studies and the present study. Moreover, the Indian population is said to have an aggressive variety of CAD, with earliest onset, multivessel involvement, and greater myocardial damage for the extent of disease.

### Symptoms and Signs

Chest pain was the most common symptom overall and was noted in 193 (98.4%) patients without blocks and 29 (80.5%) patients with blocks. Vomiting and giddiness are the next two common symptoms. Breathlessness, palpitations, vomitings, and giddiness were more common in patients with CB compared to those without CB which was statistically significant.

The probable reason for more breathlessness and other symptoms could be explained by the severity of the nature of disease. Patients with CB predominantly had anterior wall involvement (22/36, 61%). Therefore, these patients are bound to have large areas of myocardium at risk, more significant LV dysfunction. Hence, these patients were likely to have symptoms of low cardiac output such as breathlessness, palpitations, vomitings, and giddiness. Furthermore, the patients were much sicker with significant mortality and renal dysfunction.

### Cardiogenic Shock

Cardiogenic shock was more common in patients with CB (38.8%) than in those without in the present study (13.2%). The incidence of cardiogenic shock was 100% in patients with CHB in the present study, which was higher on comparison with other studies.

Shirafkan *et al.* in their study showed that all patients with first-degree AVB were discharged alive, whereas 2/3 of patients who developed CHB died. Similarly, Nguyen *et al.*, in their study, showed that patients with AMI who developed third-degree heart block had greater in-hospital mortality than did those who did not develop CHB (43.2% vs. 13.0%). This shows that patients with CHB are quite sick and are bound to have significant mortality and morbidity and hence the significant amount of hypotension

### Mortality

In patients with CB, the mortality rate was higher (33.3%) than in those without (10.2%). Values obtained are higher in the present study on comparison with all other studies. This could be due to the most severe nature of CAD which is usually seen in Indian patients.

In Indians, the CAD is considered to start a decade earlier, and the incidence of multivessel disease is also high. Moreover, the Indian patients are known to have much severe disease compared to lesion severity, in the form of significant myocardial damage, lower ejection fractions,

higher morbidity and mortality for the same amount of disease. This could very well explain the higher mortality rates in the present study.

Furthermore, factors relating to delay in coming to medical attention, as well as a delay in treatments and lack of awareness among patients, could also have resulted in higher mortality.

## CONCLUSION

1. Developing heart block is an indirect measure of the severity and extension of the disease in patients with AMI.
2. CB are associated with higher in-hospital mortality rate and are important predictors of poor outcome in patients with AMI.

## LIMITATIONS

1. One of the main drawbacks of our study was the fact that there was approximately 2.5 h lag between the onset of the patients' symptoms and the recording of the baseline ECG. There is a strong possibility of developing heart block during this lag period, and such heart blocks would have been considered as "old" heart blocks and excluded from the study.
2. The other drawback of the study was the fact that due to certain limitations the patients were not followed up after discharge from the hospital.

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# Regional Clinical Profile and Predictors of Thrombocytopenia in Adults with Dengue Fever

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## Abstract

**Introduction:** Dengue is caused by dengue virus (DENV) 1-4. *Aedes aegypti* mosquito is the predominant vector. Dengue is one of the most important arthropod-borne diseases worldwide, with estimated 50-100 million cases per year. Dengue epidemics are frequent in India. Most of the dengue viral infections are self-limiting, but complications can result in high morbidity and mortality.

**Aims and Objectives:** (1) To study the regional clinical profile for dengue fever. (2) To assess if any clinical parameter can be used as a predictor for thrombocytopenia and platelet transfusion.

**Materials and Methods:** A total of 100 patients admitted to Government Medical College, Ernakulam during 2014-2015, were studied. This is a prospective observational cohort study. The SPSS software (version 22) was used for analysis of data, and descriptive statistics were calculated.

**Results:** In our study of 100 patients, the mortality was nil. A significant incidence of thrombocytopenia was seen in patients with a second spike of fever ( $P = 0.001$ , linear association = 0.041). Patients with a second spike of fever had a significant incidence of needing platelet transfusions as opposed to those cases with no second fever spike ( $P = 0.041$ , linear association = 0.003). An increase of serum glutamic oxaloacetic transaminase (SGOT)/serum glutamic pyruvic transaminase (SGPT) >40 was associated with an increased incidence of platelet transfusion with statistical significance (SGOT:  $P = 0.004$ , linear association = 0.001), (SGPT:  $P = 0.034$ , linear association = 0.001). 23% of the study population showed electrocardiogram (ECG) changes. The presence of ECG changes had a statistically significant association with thrombocytopenia ( $P = 0.035$ ). A positive dengue immunoglobulin G antibody (IgGAb) was associated with an increased incidence of thrombocytopenia with statistical significance ( $P = 0.021$ ), whereas immunoglobulin M antibody showed no statistical significance ( $P = 0.352$ ).

**Conclusion:** We conclude that routine clinical parameters such as second spike of fever and routine clinical parameters such as platelet count on seeing the patient, liver enzymes (SGOT/SGPT), and erythrocyte sedimentation rate as well as dengue IgGAb when available could be used as useful indicators to predict patient who are at higher risk in having morbidities due to dengue infection.

**Key words:** Dengue fever, Thrombocytopenia, Predictors, Profile

## INTRODUCTION

Dengue is caused by dengue virus (DENV) 1-4. *Aedes aegypti* mosquitoes are the predominant vector. Dengue is one of the most important arthropod-borne diseases

worldwide, with estimated 50-100 million cases per year.<sup>1</sup> A larger population of people are vulnerable to dengue due to international travel and spreading of mosquitoes from tropical countries to nontropical areas. The World Health Organization estimates that almost half the world's population lives in countries where dengue is endemic. Dengue epidemics are frequent in India. Most of the dengue viral infections are self-limiting, but complications can result in high morbidity and mortality.<sup>2,3</sup>

The dengue epidemic which has a seasonal recurrence is growing in magnitude as of recently. It has become one of the major causes of fever in inpatients as well

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as outpatients causing unprecedented panic among the general population. Thus, DENV remains a major cause of morbidity and mortality in tropical areas.<sup>4,6</sup>

This prospective study was designed to build the clinical profile of 100 cases of dengue fever attending a tertiary care center in South India. There is a lot of panic regarding the platelet counts in dengue season. Any patient of fever causes panic among the patient and relatives about possibility of thrombocytopenia. Thrombocytopenia is an important pointer to the diagnosis of dengue for the lay-person and the general physician. We attempt to find if any clinical parameter can be used as a predictor thrombocytopenia/platelet transfusion which will be particularly useful in referring a patient to a tertiary care setting.

### Aims and Objectives

1. To establish a regional clinical profile for dengue fever.
2. To assess if any clinical parameter can be used as a predictor for thrombocytopenia/platelet transfusion.

## MATERIALS AND METHODS

This is a prospective observational study done on patients admitted to the Government Medical College, Ernakulam, in the 2014-2015 period with dengue fever. The diagnosis of dengue infection was made clinically on the basis of fever, myalgia, and skin rash during an epidemic and confirmed by laboratory investigation. All patients with acute febrile illness underwent NS1 Ag and serology (immunoglobulin M [IgM] and immunoglobulin G [IgG]) by IVD microwell ELISA. Other causes of thrombocytopenia such as chronic liver diseases and idiopathic thrombocytopenic purpura were not excluded in all cases.

The patients were subjected to a thorough clinical examination, and a structured pro forma was filled in for each case. They underwent investigations such as complete hemogram, urea, creatinine, liver function tests, chest X-ray, electrocardiogram (ECG), and serum electrolytes.

The SPSS software (version 22) was used for analysis of data. Descriptive statistics were calculated. Numbers and percentages were enumerated for all categorical variables such as clinical characteristics and biochemical tests.

### Limitations

Dengue fever being seasonal in occurrence the cases over a year span of 2014-2015 were chosen for the study. More parameters could not be included in the study. A more detailed study on a larger population is warranted spread over a longer period.

## RESULTS

In our study, the main age group affected was between 20 and 49 constituting 69% of the total study group (Table 1). 22% of the population had other co-infections. The mean duration of fever on presentation to the hospital was  $3.23 \pm 0.649$  days (Table 2). 75% of patients presented with mild to moderate grades of fever. 25% had high-grade fever (Table 3). The second spike of fever was seen in 14% of the study population (Table 4). 25% showed no thrombocytopenia ( $>100,000$ ). 35% had a platelet count of  $<100,000$ ; 26% had counts  $<50,000$ . Only 14% of the study population had a platelet count  $<20,000$  (Table 5). 23% of the study population required platelet transfusion (Table 9).

**Table 1: The age category**

Age	Frequency	Percent	Valid percent	Cumulative percent
Valid				
10-19	15	15.0	15.0	15.0
20-29	41	41.0	41.0	56.0
30-39	17	17.0	17.0	73.0
40-49	12	12.0	12.0	85.0
50-59	6	6.0	6.0	91.0
60-69	5	5.0	5.0	96.0
70+	4	4.0	4.0	100.0
Total	100	100.0	100.0	

**Table 2: Fever duration**

Duration of fever	Number	Minimum	Maximum	Mean $\pm$ Standard deviation
Duration of fever	100	3	7	3.23 $\pm$ 0.649
Valid number (list wise)	100			

**Table 3: Grade of fever**

Grade of fever	Frequency	Percent	Valid percent	Cumulative percent
Valid				
Mild	42	42.0	42.0	42.0
Moderate	33	33.0	33.0	75.0
High	25	25.0	25.0	100.0
Total	100	100.0	100.0	

**Table 4: Second spike of fever**

Second spike	Frequency	Percent	Valid percent	Cumulative percent
Valid				
NA	86	86.0	86.0	86.0
<3 days	11	11.0	11.0	97.0
4-7 days	3	3.0	3.0	100.0
Total	100	100.0	100.0	

There was a significant association both statistical as well as linear between the units of platelet transfusions required and degree of thrombocytopenia ( $P = 0.006$ , linear association = 0.001). A significant incidence of thrombocytopenia was seen in patients with a second spike of fever ( $P = 0.001$ , linear association = 0.041) (Table 6). Patients with a second spike of fever had a significant incidence of needing platelet transfusions as opposed to those cases with no second fever spike ( $P = 0.041$ , linear association = 0.003) (Table 10). Although not statistically significant, mild to moderate increase of serum glutamic oxaloacetic transaminase (SGOT)/serum glutamic pyruvic transaminase (SGPT) (40-500) (Tables 6-8) was seen in 81% and 79% of the study population, respectively. Of the 14 cases with 2<sup>nd</sup> spike of fever, 12 patients had elevated SGOT/SGPT levels >40, but no statistical significance could be proven; possibly due to the reduced numbers of patients with second fever spike as compared to the study population (Tables 11 and 12). An increase of SGOT/

SGPT >40 was associated with an increased incidence of platelet transfusion with statistical significance. (SGOT:  $P = 0.004$ , linear association = 0.001) (SGPT:  $P = 0.034$ , linear association = 0.001) (Tables 13 and 14). A positive dengue IgG antibody (Ab) was associated with an increased incidence of thrombocytopenia with statistical significance ( $P = 0.021$ ) (Table 15), whereas IgMAB showed no statistical significance ( $P = 0.352$ ) (Table 16). However, IgGAb showed no statistical association with units of platelets transfused ( $P = 0.554$ ). 23% of the study population showed ECG changes. The presence of ECG changes (Table 17) had a statistically significant association with thrombocytopenia ( $P = 0.035$ ). A low erythrocyte sedimentation rate (ESR) of <20 mm showed a non-linear statistically significant association with the units of platelets transfused ( $P = 0.036$ ); but no statistical correlation with thrombocytopenia ( $P = 0.563$ ) (Tables 18 and 19). Lymphocytosis showed no correlation with either thrombocytopenia or platelet transfusions ( $P = 0.837$ ;  $P = 0.196$ ). In our case study of 100 patients, the mortality was nil.

**Table 5: Incidence of thrombocytopenia**

Thrombocytopenia	Frequency	Percent	Valid percent	Cumulative percent
Valid				
No	25	25.0	25.0	25.0
<1 lakh	35	35.0	35.0	60.0
<50,000	26	26.0	26.0	86.0
<20,000	14	14.0	14.0	100.0
Total	100	100.0	100.0	

**Table 6: Thrombocytopenia versus 2<sup>nd</sup> spike of fever (cross tabulation)**

Thrombocytopenia	2 <sup>nd</sup> spike of fever			Total
	NA	<3 days	4-7 days	
No				
Count	23	0	2	25
% of total	23.0	0.0	2.0	25.0
<1 lakh				
Count	30	5	0	35
% of total	30.0	5.0	0.0	35.0
<50,000				
Count	26	0	0	26
% of total	26.0	0.0	0.0	26.0
<20,000				
Count	7	6	1	14
% of total	7.0	6.0	1.0	14.0
Total				
Count	86	11	3	100
% of total	86.0	11.0	3.0	100.0

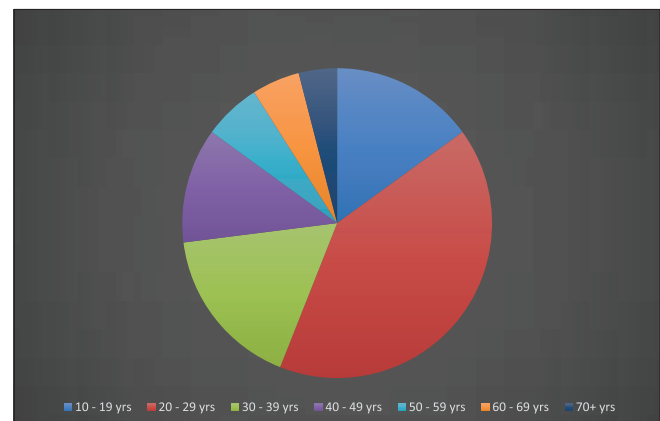
Chi-square tests			
	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-square	26.392 <sup>a</sup>	6	0.001
Likelihood ratio	27.745	6	0.001
Linear-by-linear association	4.173	1	0.041
Number of valid cases	100		

Critical value: >16.8

## DISCUSSION

Our study aimed at establishing a regional clinical profile for patients with dengue fever. We attempted to ascertain if any clinical parameter could be used as an indicator for the patient developing thrombocytopenia. Such a parameter could be of use in peripheral setups to pick the subset of patients who could be at risk for developing thrombocytopenia.

In our study, dengue fever was distributed more among the young and middle-aged population with 69% of the affected patients falling in the age group between 20 and 49 (Figure 1). In a similar study by Aroor *et al.*, 87 patients (42%) were in the age group of 18-30 years.<sup>7</sup> Munir *et al.* found that most cases were between 20 and 49 years of age.<sup>8</sup>



**Figure 1: Age distribution**

**Table 7: Thrombocytopenia versus SGOT cross tabulation**

Thrombocytopenia	SGOT						Total
	ND	<40	40-100	100-500	500-1000	More than 1000	
No							
Count	2	2	13	7	1	0	25
% of total	2.0	2.0	13.0	7.0	1.0	0.0	25.0
<1 lakh							
Count	2	2	21	9	1	0	35
% of total	2.0	2.0	21.0	9.0	1.0	0.0	35.0
<50,000							
Count	0	3	13	8	2	0	26
% of total	0.0	3.0	13.0	8.0	2.0	0.0	26.0
<20,000							
Count	0	2	5	5	1	1	14
% of total	0.0	2.0	5.0	5.0	1.0	1.0	14.0
Total							
Count	4	9	52	29	5	1	100
% of total	4.0	9.0	52.0	29.0	5.0	1.0	100.0

SGOT: Serum glutamic oxaloacetic transaminase

**Chi-square tests**

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-square	12.495 <sup>a</sup>	15	0.641
Likelihood ratio	11.661	15	0.704
Linear-by-linear association	2.846	1	0.092
Number of valid cases	100		

Critical value: &gt; 12.511

**Table 8: Thrombocytopenia versus SGPT cross tabulation**

Thrombocytopenia	SGPT					Total
	ND	<40	40-100	100-500	500-1000	
No						
Count	2	2	17	4	0	25
% of total	2.0	2.0	17.0	4.0	0.0	25.0
<1 lakh						
Count	2	6	18	9	0	35
% of total	2.0	6.0	18.0	9.0	0.0	35.0
<50,000						
Count	0	5	11	10	0	26
% of total	0.0	5.0	11.0	10.0	0.0	26.0
<20,000						
Count	0	3	5	5	1	14
% of total	0.0	3.0	5.0	5.0	1.0	14.0
Total						
Count	4	16	51	28	1	100
% of total	4.0	16.0	51.0	28.0	1.0	100.0

SGPT: Serum glutamic pyruvic transaminase

**Chi-square tests**

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-square	15.565 <sup>a</sup>	12	0.212
Likelihood ratio	14.961	12	0.244
Linear-by-linear association	2.774	1	0.096
Number of valid cases	100		

Critical value: &gt; 15.605

Kumar *et al.* reported the most common symptoms in their study as fever, myalgia, vomiting, headache, and abdominal pain, and the most common hemorrhagic manifestation was petechiae, and they recorded in

their study 83.9% cases dengue fever, 8.8% dengue hemorrhagic fever (DHF), and 7.3% dengue shock syndrome (DHS).<sup>9</sup> In children, if symptoms such as fever, pain, rashes, and vomiting are associated with hepatomegaly and elevated SGOT in the context of low total platelet count, a strong possibility of dengue fever is present, especially in an epidemic setting. Early suspicion and effective management can reduce the severity.<sup>10</sup> In our study group, only classical dengue cases were found. No case of DHF or DHS was observed.

In the study conducted by Aroor *et al.*, abdominal symptoms such as nausea and vomiting (53.6%), abdominal pain (25.1%), and diarrhea (13.5%) were present.<sup>7</sup> However, these symptoms were not prominent in our patients.

In our study, 75% of the population had thrombocytopenia (platelet count <100,000/mm<sup>3</sup>); and 14% had a count <20,000/mm<sup>3</sup> on admission. 23% required platelet transfusion during their hospital stay. Jayanthi *et al.* found that platelet count could be used to predict the complication and duration of hospital stay and hence better use of resources.<sup>11</sup>

In our study, the second spike of fever was seen in 14% of the population. A significant incidence of thrombocytopenia was seen in patients with a second spike of fever ( $P = 0.001$ , linear association = 0.041) (Figure 2). Patients with a second spike of fever needed platelet transfusions as well as more units of platelets compared to

**Table 9: Thrombocytopenia\*Platelet transfusion cross tabulation**

Thrombocytopenia	Platelet transfusion										Total
	No	1 U platelet concentration	2 U platelet concentration	4 U platelet concentration	5 U platelet concentration	6 U platelet concentration	7 U platelet concentration	8 U platelet concentration	10 U platelet concentration	12 U platelet concentration	
No	19	1	0	2	2	0	0	1	0	0	25
<1 lakh	28	0	1	1	0	4	0	1	0	0	35
<50,000	17	0	1	5	0	2	0	0	0	1	26
<20,000	4	0	1	1	0	3	1	3	1	0	14
Total	68	1	3	9	2	9	1	5	1	1	100

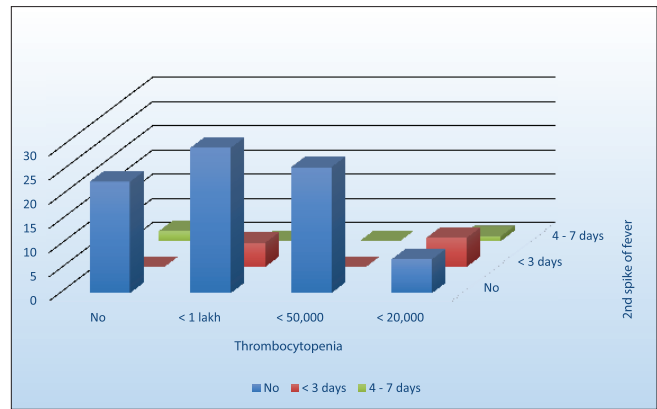
  

Chi-square tests		
	Value	df
Pearson Chi-square	48.683 <sup>a</sup>	27
Likelihood ratio	44.087	27
Linear-by-linear association	11.551	1
Number of valid cases	100	

Asymp. Sig. (2-sided)		
	0.006	
	0.020	
	0.001	

Critical value: > 46.963

**Figure 2: Second spike of fever and thrombocytopenia**

those cases with no second fever spike ( $P = 0.041$ , linear association = 0.003) (Figure 5). This observation suggests the fact that dengue associated with the second spike of fever tends to have higher morbidity (Figure 6).

There was significant statistical as well as the linear correlation between the units of platelet transfusions required and degree of thrombocytopenia ( $P = 0.006$ , linear association = 0.001) (Figure 5). Platelet transfusions do little to alleviate the thrombocytopenia in patients and have hence led to the current consensus of platelet transfusion in dengue fever induced thrombocytopenia. Aroor *et al.* found that low platelet count on admission was associated with the presence of rash, high aspartate aminotransferase (AST) and alanine aminotransferase levels, and low albumin levels.<sup>7</sup> The need for platelet transfusions was also compared with other parameters. According to current recommendations, platelet transfusions are not indicated unless the patient develops bleeding manifestations or has a high risk of life-threatening bleeds. The incidence of bleeding manifestations was nil in our study.

Aroor *et al.* found that the duration of hospital stay was longer with presence of diarrhea, abdominal pain, ascites, and low hemoglobin on admission, but it did not correlate with the platelet count on admission.<sup>7</sup>

Although not statistically significant, a mild to moderate increase of SGOT/SGPT (40-500) was seen in 81% and 79% of the study population, respectively. Of the 14 cases with a second spike of fever, 12 patients had elevated SGOT/SGPT levels >40, but no statistical significance could be proven; possibly due to the reduced numbers of patients with second fever spike as compared to the study population. An increase of SGOT/SGPT >40 was associated with an increased incidence of platelet transfusion with statistical significance (SGOT:  $P = 0.004$ , linear association = 0.001) (SGPT:  $P = 0.034$ , linear association = 0.001) (Figures 3 and 4). Senaratne

**Table 10: 2<sup>nd</sup> spike of fever versus platelet transfusion cross tabulation**

2 <sup>nd</sup> spike of fever	Platelet transfusion										Total
	No	1 U platelet concentration	2 U platelet concentration	4 U platelet concentration	5 U platelet concentration	6 U platelet concentration	7 U platelet concentration	8 U platelet concentration	10 U platelet concentration	12 U platelet concentration	
NA											
Count	62	1	3	8	2	6	0	3	0	1	86
Expected count	58.5	0.9	2.6	7.7	1.7	7.7	0.9	4.3	0.9	0.9	86.0
% of total	62.0	1.0	3.0	8.0	2.0	6.0	0.0	3.0	0.0	1.0	86.0
<3 days											
Count	5	0	0	0	0	2	1	2	1	0	11
Expected count	7.5	0.1	0.3	1.0	0.2	1.0	0.1	0.6	0.1	0.1	11.0
% of total	5.0	0.0	0.0	0.0	0.0	2.0	1.0	2.0	1.0	0.0	11.0
4-7 days											
Count	1	0	0	1	0	1	0	0	0	0	3
Expected count	2.0	0.0	0.1	0.3	0.1	0.3	0.0	0.2	0.0	0.0	3.0
% of total	1.0	0.0	0.0	1.0	0.0	1.0	0.0	0.0	0.0	0.0	3.0
Total											
Count	68	1	3	9	2	9	1	5	1	1	100
Expected count	68.0	1.0	3.0	9.0	2.0	9.0	1.0	5.0	1.0	1.0	100.0
% of total	68.0	1.0	3.0	9.0	2.0	9.0	1.0	5.0	1.0	1.0	100.0
Chi-square tests											
		Value		df		Asymp. Sig. (2-sided)					
Pearson Chi-square		29.619 <sup>a</sup>		18		0.041					
Likelihood ratio		21.261		18		0.266					
Linear-by-linear association		8.593		1		0.003					
Number of valid cases		100									
Critical value: >29.6492											

**Table 11: SGOT versus 2<sup>nd</sup> spike of fever**

SGOT	2 <sup>nd</sup> spike of fever			Total
	NA	<3 days	4-7 days	
ND				
Count	3	1	0	4
% of total	3.0	1.0	0.0	4.0
<40				
Count	8	1	0	9
% of total	8.0	1.0	0.0	9.0
40-100				
Count	44	6	2	52
% of total	44.0	6.0	2.0	52.0
100-500				
Count	26	2	1	29
% of total	26.0	2.0	1.0	29.0
500-1000				
Count	4	1	0	5
% of total	4.0	1.0	0.0	5.0
More than 1000				
Count	1	0	0	1
% of total	1.0	0.0	0.0	1.0
Total				
Count	86	11	3	100
% of total	86.0	11.0	3.0	100.0

SGOT: Serum glutamic oxaloacetic transaminase

**Chi-square tests**

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-square	2.528 <sup>a</sup>	10	0.990
Likelihood ratio	3.003	10	0.981
Linear-by-linear association	0.184	1	0.668
Number of valid cases	100		

Critical value: &gt; 2.558

**Table 12: SGPT versus 2<sup>nd</sup> spike of fever**

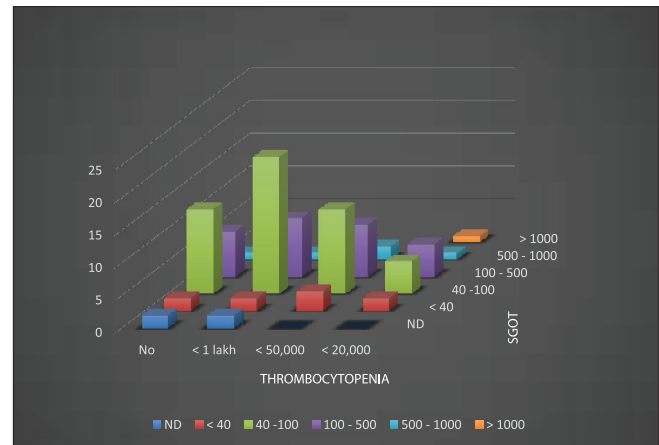
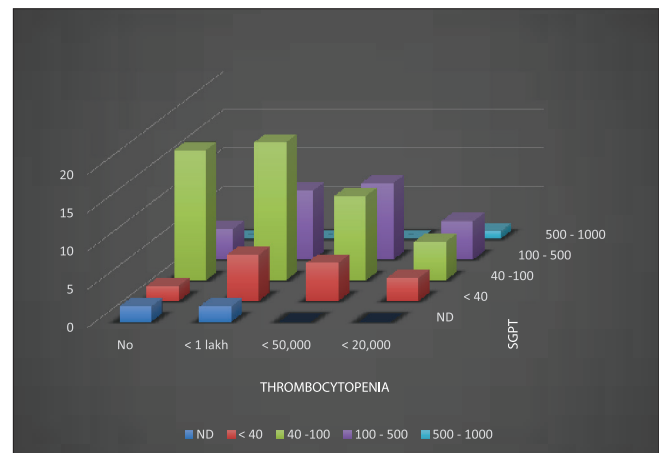
SGPT	2 <sup>nd</sup> spike of fever			Total
	NA	<3 days	4-7 days	
ND				
Count	3	1	0	4
% of total	3.0	1.0	0.0	4.0
<40				
Count	15	1	0	16
% of total	15.0	1.0	0.0	16.0
40-100				
Count	43	6	2	51
% of total	43.0	6.0	2.0	51.0
100-500				
Count	24	3	1	28
% of total	24.0	3.0	1.0	28.0
500-1000				
Count	1	0	0	1
% of total	1.0	0.0	0.0	1.0
Total				
Count	86	11	3	100
% of total	86.0	11.0	3.0	100.0

SGPT: Serum glutamic pyruvic transaminase

**Chi-square tests**

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-square	2.193 <sup>a</sup>	8	0.975
Likelihood ratio	2.786	8	0.947
Linear-by-linear association	0.021	1	0.885
Number of valid cases	100		

Critical value: &gt; 2.310

**Figure 3: Serum glutamic oxaloacetic transaminase versus thrombocytopenia****Figure 4: Serum glutamic pyruvic transaminase versus thrombocytopenia**

*et al.* found that AST and ALT levels correlate with both disease severity and circulating interleukin-2 levels.<sup>12</sup> This statistical significance to platelet transfusion and not to thrombocytopenia could be explained by the fact that not all patients with thrombocytopenia developed bleeding manifestations. Those subsets of patients who had low platelet count ( $<20,000/\text{mm}^3$ ) tend to require more units of platelet transfusions.

A positive dengue IgGAb was associated with an increased incidence of thrombocytopenia with statistical significance ( $P = 0.021$ ); whereas IgMAb showed no statistical significance ( $P = 0.352$ ). However, IgGAb showed no statistical association with units of platelets transfused ( $P = 0.554$ ). This is supportive of the fact that the second infection with another strain tends to develop thrombocytopenia more frequently.

About 23% of the study population showed ECG changes. The presence of ECG changes had a statistically significant association with thrombocytopenia ( $P = 0.035$ ). However,



SGPT	Platelet transfusion	Total
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Chi-square tests		
	Value	df
Pearson Chi-square	52.956 <sup>a</sup>	36
Likelihood ratio	42.587	36
Linear-by-linear association	16.631	1
Number of valid cases	100	

a. Critical value: > 52.946

**Table 15: IgGAb versus thrombocytopenia cross tabulation**

IgGAb	Thrombocytopenia				Total
	No	<1 lakh	<50,000	<20,000	
Negative					
Count	19	25	23	6	73
% of total	19.0	25.0	23.0	6.0	73.0
Positive					
Count	6	10	3	8	27
% of total	6.0	10.0	3.0	8.0	27.0
Total					
Count	25	35	26	14	100
% of total	25.0	35.0	26.0	14.0	100.0

IgGAb: Immunoglobulin G antibody

**Chi-square tests**

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-square	9.765 <sup>a</sup>	3	0.021
Likelihood ratio	9.501	3	0.023
Linear-by-linear association	1.362	1	0.243
Number of valid cases	100		

Critical value: &gt; 9.730

**Table 16: IgMAb versus thrombocytopenia cross tabulation**

IgMAb	Thrombocytopenia				Total
	No	<1 lakh	<50,000	<20,000	
Negative					
Count	15	22	20	7	64
% of total	15.0	22.0	20.0	7.0	64.0
Positive					
Count	10	13	6	7	36
% of total	10.0	13.0	6.0	7.0	36.0
Total					
Count	25	35	26	14	100
% of total	25.0	35.0	26.0	14.0	100.0

IgMAb: Immunoglobulin M antibody

**Chi-square tests**

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-square	3.269 <sup>a</sup>	3	0.352
Likelihood ratio	3.355	3	0.340
Linear-by-linear association	0.008	1	0.927
Number of valid cases	100		

Critical value: &gt; 3.283

the changes seen were non-specific and were not indicative of myocarditis ECG wise or clinically. Kularatne *et al.* have recorded in their study that 62.5% of their patients had ECG changes (T inversion, ST depression, bundle branch blocks).<sup>13</sup>

A low ESR of <20 mm showed a non-linear statistically significant association with the units of platelets transfused ( $P = 0.036$ ); but no statistical correlation with thrombocytopenia ( $P = 0.563$ ). Lymphocytosis showed no correlation with either thrombocytopenia or platelet transfusions ( $P = 0.837$ ;  $P = 0.196$ ). Souza *et al.* in their study found that ESR was within normal ranges

**Table 17: ECG changes versus thrombocytopenia cross tabulation**

ECG changes	Thrombocytopenia				Total
	No	<1 lakh	<50,000	<20,000	
ND	2	0	0	0	2
Absent	16	31	16	12	75
Present	7	4	10	2	23
Total	25	35	26	14	100

ECG: Electrocardiogram

**Chi-square tests**

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-square	13.579 <sup>a</sup>	6	0.035
Likelihood ratio	13.193	6	0.040
Linear-by-linear association	0.413	1	0.520
Number of valid cases	100		

Critical value: &gt; 13.556

**Table 18: Low ESR versus thrombocytopenia**

Low ESR	Thrombocytopenia				Total
	No	<1 lakh	<50,000	<20,000	
Normal/High	3	5	5	4	17
Low	22	30	21	10	83
Total	25	35	26	14	100

ESR: Erythrocyte sedimentation rate

**Chi-square tests**

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-square	2.046 <sup>a</sup>	3	0.563
Likelihood ratio	1.915	3	0.590
Linear-by-linear association	1.829	1	0.176
Number of valid cases	100		

Critical value: &gt; 2.060

in most dengue cases, independent of gender or clinical presentation.<sup>14</sup>

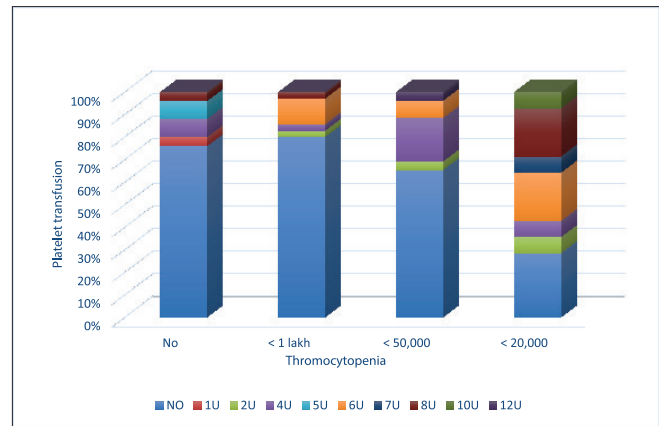
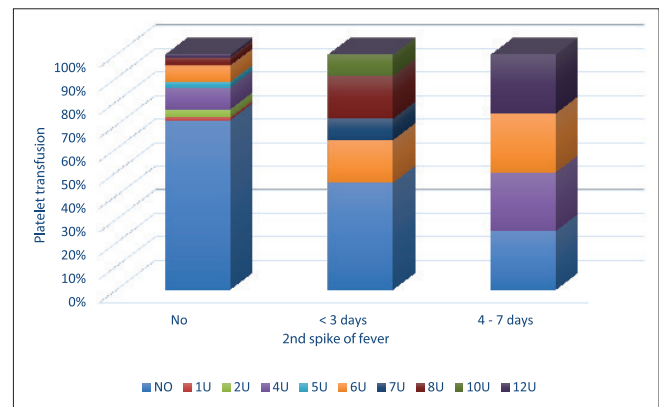
Pone *et al.* reported in their study lethargy, abdominal distension, pleural effusion, and hypoalbuminemia as the best clinical and laboratorial markers of serious dengue disease in hospitalized children.<sup>15</sup> However, these were not recorded in our study in the mentioned age group.

In the study conducted by Aroor *et al.*, they concluded that though thrombocytopenia on admission was associated with the presence of rash, high AST and ALT levels, and low albumin levels, it was not predictive of length of hospitalization and duration of hospital stay was longer with the presence of diarrhea, abdominal pain, ascites, and low hemoglobin level on admission.<sup>7</sup>

There was no mortality our study group. Munir *et al.* reported from Pakistan, a mortality rate of 0.6% in admitted cases of dengue, conducted at five tertiary care hospitals.<sup>8,16-18</sup> Total number of deaths was 110 all over India in 2010 (mortality 0.4% of 28,066 cases).<sup>9</sup>

**Table 19: Low ESR versus platelet transfusion**

Low ESR												Total
No	1 U platelet concentration	2 U platelet concentration	4 U platelet concentration	5 U platelet concentration	6 U platelet concentration	7 U platelet concentration	8 U platelet concentration	10 U platelet concentration	12 U platelet concentration			
11	0	3	2	0	0	0	1	0	0	17		
57	1	0	7	2	9	1	4	1	1	83		
68	1	3	9	2	9	1	5	1	1	100		
ESR: Erythrocyte sedimentation rate												
Chi-square tests												
		Value		df		Asymp. Sig. (2-sided)						
Pearson Chi-square		17.958 <sup>a</sup>		9		0.036						
Likelihood ratio		16.447		9		0.058						
Linear-by-linear association		0.528		1		0.468						
Number of valid cases		100										
Critical value: > 17.929												

**Figure 5: Thrombocytopenia versus platelet transfusion****Figure 6: Second spike of fever versus platelet transfusion**

## CONCLUSION

A significant association of thrombocytopenia was seen in patients with a second spike of fever as well as a positive IgGAb. Greater units of platelet transfusions were required in patients with a second spike of fever, thrombocytopenia on admission to the hospital, an increase of SGOT/SGPT more than 40 and a low ESR of <20 mm.

We conclude that routine clinical parameters such as second spike of fever and routine clinical parameters such as platelet count on seeing the patient, liver enzymes (SGOT/SGPT), and ESR as well as dengue IgGAb when available could be used as useful indicators to predict patient who are at higher risk in having morbidities due to dengue infection.

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# Efficacy of Diagnosing Vascular Occlusion in Diabetic Foot Patients to Improve the Outcome

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## Abstract

**Introduction:** Peripheral artery occlusive disease (PAOD) is a manifestation of atherosclerosis characterized by atherosclerotic occlusive disease of the lower extremities and is a marker for atherothrombotic disease in other vascular beds. PAOD is also a major risk factor for lower-extremity amputation, especially in patients with diabetes.

**Aim:** To study the efficacy of diagnosing vascular occlusion and to improve the treatment outcome in diabetic ulcer foot patients.

**Methods:** Prospective study was conducted to predict the outcome of diabetic foot patients using ankle-brachial index (ABI) and toe-brachial index (TBI).

**Results:** A total of 19 patients underwent amputation in both minor/major. 4 patients had duplex ultrasonography proven arterial occlusion/stenosis and rest of 15 patients had diffuse arteriosclerosis. Among the 15 patients with diffuse arterial disease, 5 patients had normal ABI. All these 5 patients had very low TBI suggesting TBI is a better indicator of amputation in diabetic foot patient according to the study.

**Conclusion:** Toe-brachial pressure index is a better index to diagnosis PAOD in diabetic ulcer foot patient, compared to ABI.

**Key words:** Amputation, Diabetic ulcer foot, Peripheral artery occlusive disease

## INTRODUCTION

Peripheral artery occlusive disease (PAOD), referred to as peripheral arterial disease (PAD) or peripheral vascular disease (PVD), refers to the obstruction or deterioration of arteries other than those supplying the heart and within the brain.<sup>1</sup> The risk of PAD is markedly increased among individuals with diabetes, and ischemic event rates are higher in diabetic individuals with PAD than in comparable non-diabetic populations. PVD is common among patients with diabetes. An increase in hemoglobin A1c by 1% can result in more than a 25% risk of PAD.<sup>2</sup> Major amputation rates are 5-10 times higher in diabetics than non-diabetics.<sup>3</sup> Because of these causal relations,

the American Diabetes Association recommends ankle-brachial index (ABI) screening every 5 years in patients with diabetes. The care of diabetic patients should start with preventive measures, and it is important to avoid infections in patients with insensate feet because of neuropathy.<sup>4</sup> These patients need to wear properly fitted shoes at all times for protection. Orthotic inserts should be used to distribute weight evenly to avoid pressure on the metatarsal heads of the foot. Diabetic patients may be unaware of the presence of infections or ulcerative lesions because of peripheral neuropathy and a decreased ability to sense pain. In this population, infections can progress rapidly, with significant tissue damage from a combination of delayed presentation and compromised immune function. On presentation, a careful physical examination is important to plan for appropriate treatment. The overlying cellulitis is assessed, and any possible underlying abscess is examined by palpation for crepitus or detection of drainage of purulent fluid. Cellulitis should not be confused with dependent rubor caused by severe ischemia in patients with PAD.<sup>5</sup> The presence of an abscess requires immediate drainage before revascularization. The status of arterial

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circulation is documented. The presence or absence of lower-extremity pulses in the common femoral, popliteal, and pedal arteries is examined. The pulses may be difficult to palpate because of swelling from foot infection; non-invasive arterial ultrasound can be useful in assessing the extent of arterial disease. Insulin-dependent diabetic patients may have calcified walls of the medium and small arteries that can falsely elevate the segmental pressures of the leg. In this situation, digital pressures of the toes can be accurately measured and a pressure higher than 30 mm Hg is predictive of healing after local amputation and debridement.<sup>6</sup> Plain X-rays with multiple views of the foot can assist in assessing the extent of foot infection. Gas in soft tissue signifies deep tissue infection and the need for surgical débridement. Advanced osteomyelitis can be seen; however, plain films may not show early bone infection. Magnetic resonance imaging of the foot is a sensitive imaging modality for detecting soft tissue infection and early bone infection. Routine laboratory work is sent and evaluated for subtle signs of sepsis. Sudden worsening of glycemic control or a rise in creatinine level is seen frequently, often without an increase in leukocytes.<sup>7</sup> In infections with only cellulitis and no underlying soft tissue involvement, patients are treated with intravenous antibiotic therapy. If the cellulitis does not resolve in several days, there may not be adequate antibiotic coverage and the presence of deep tissue infection is considered. The choice of the antibiotics used and the foot need to be reevaluated; reimaging the foot may be necessary. The cause of persistent cellulitis and non-healing sepsis is usually underlying deep infection or osteomyelitis. Other patients may present with gangrene, open joint or exposed bone, or abscess. In these patients, surgical débridement and drainage are required in addition to antibiotic therapy. Small open wounds can be treated with simple débridement and drainage, but often there is deep tissue involvement that is not visible on the surface. To remove all non-viable tissue and wide drainage, amputation may be required. If there is extensive infection of the foot with gas, calf pain, or systemic sepsis, the patient may require amputation as initial therapy. After surgical débridement and drainage, patients are treated with aggressive wound care using dressing changes and continued broad-spectrum antibiotic therapy until intraoperative culture sensitivities are finalized and allow for the use of targeted antimicrobials. Wounds are evaluated closely for persistent infection that may require additional surgical intervention. In patients with adequate arterial circulation, the wound can be closed secondarily after resolution of the infection. All patients with evidence of concomitant arterial occlusive disease are considered for lower-extremity revascularization with open bypass surgery or endovascular stenting or angioplasty to optimize wound healing and limb salvage.<sup>8-13</sup>

## Aim

To study the efficacy of diagnosing vascular occlusion and to improve the treatment outcome in diabetic ulcer foot patients.

## MATERIALS AND METHODS

A prospective study was conducted in the Department of General Surgery and Vascular Surgery at Government Rajaji Hospital, Madurai. The Ethics Committee approval and informed consent was obtained. The patient from both gender and age more than 18 years were screened. Patients with diabetic ulcer foot more than Grade 2 as per the University of Texas Grading System were included in the study. Known cases of PVDs are excluded from the study. The study patients demographic details with history of diabetes were collected. All patients were subjected to clinical examination, ABI measurement, toe pressure measurement, and arterial ultrasound Doppler study of both lower limbs. Patients were assessed after 1 month of the first visit.

## RESULTS

In this study of 100 patients, 19 females and 81 males were included. 41-50 years of age group had the highest number of patients 48% (Table 1).

In Grade 2 ulcer patients, 29 patients had infection and 5 patients had ischemia. In Grade 3 ulcer patients, 71 patients had infection and 5 patients had ischemia (Table 2). Out of the 100 patients, 75 patients did not have pain. 25 patients had pain in lesion and on walking showing that patients with diabetic foot in addition have peripheral neuropathy. So, pain perception is less.

**Table 1: Distribution study patients in age group**

Age distribution	Number of patients (%)
31-40	7 (7)
41-50	48 (48)
51-60	22 (22)
61-70	11 (11)
71-80	12 (12)

**Table 2: Distribution of study patients in ulcer grading**

Ulcer grading	Number of patients with infection	Number of patients with ischemia
Grade 2	29	5
Grade 3	71	5

Duplex Doppler of both lower limb showed diffuse atherosclerosis in 95 patients and occlusion/stenosis in 5 patients; all had pathology in the popliteal artery (Table 3).

After 1 month follow-up, 19 patients were subjected for minor and major amputation, 31 patients were on regular wound debridement and dressing, 49 patients underwent grafting, and 1 patient expired. 84% of patients are palpable, 14% had absent dorsalis pedis artery followed by posterior tibial artery 2% (Table 4).

The prediction of outcome comparing ankle-brachial index and toe brachial index has shown a reasonably significant difference i.e., toe-brachial index predicted the disease outcome better than ankle-brachial index. TBI predicted the disease outcome better than ABI (Table 5).

19 patients underwent amputation in both minor/major. 4 patients had duplex ultrasonography proven arterial occlusion/stenosis and rest of 15 patients had diffuse arteriosclerosis. Among the 15 patients with diffuse arterial disease, 5 patients had normal ABI. All these 5 patients had very low TBI suggesting TBI is a better indicator of amputation in diabetic foot patient according to the study (Figure 1).

## DISCUSSION

Pilot study of the prevalence of asymptomatic peripheral arterial occlusive disease in patients with diabetes by Elhadd *et al.*<sup>14</sup> suggested the prevalence of asymptomatic PAOD in diabetic foot patients in their study cohort was 33%. In this study, around 20% had PAOD, diagnostic criteria were ABI <0.9, TBI <0.6, duplex ultrasound proven arterial occlusive disease. In our study, 20 patients had low TBI, and 5 patients had Duplex ultrasound proven PAOD. All these patients were started on antiplatelet agents, lipid lowering agents and referred to vascular surgery department for further management and revascularization procedure after amputation of gangrenous segments of the foot. Steven and William suggested<sup>15</sup> cigarette smoking is the most important risk factor for the development and progression of PAD. The amount and duration of tobacco use correlate directly with the development and progression of PAD in diabetic foot patients smoking cessation increases long-term survival in patients with PAD. In one study, the 10-year survival rate was 82% in former smokers compared with 46% in continuing smokers. In this study, 80% patients were smokers. Steven and William<sup>15</sup> suggested hypertension increases the high risk of cardiovascular disease associated with diabetes. However, the role of intensive blood pressure control in patients with diabetes and PAD has not been established.

**Table 3: Doppler study results**

Doppler study	Number of patients (%)
Diffuse atherosclerosis	95 (95)
Occlusion/stenosis	5 (5)

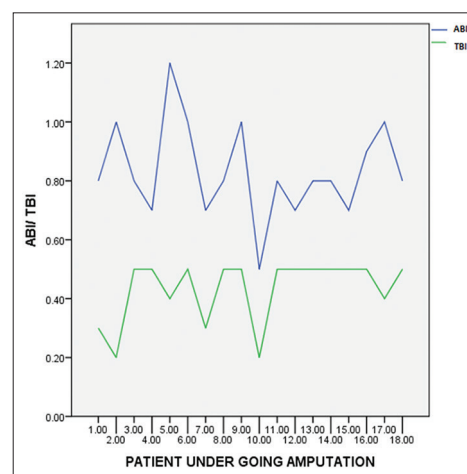
**Table 4: Pulse status of the lower limbs**

Pulse status	Number of patients (%)
Absent dorsalis pedis artery	14 (14)
Absent posterior tibial artery	2 (2)
All palpable	84 (84)

**Table 5: Comparison of ABI and TBI**

Doppler finding	Mean value	
	ABI	TBI
Diffuse	1.07	0.75
Popliteal occlusion	0.51	0.19
Popliteal stenosis	0.71	0.44

ABI: Ankle-brachial index, TBI: Toe-brachial index



**Figure 1: Variations in ABI and TBI among individual patient who had undergone amputation (ABI- Ankle-brachial index, TBI- Toe-brachial index)**

In a recent study, blood-pressure lowering in normotensive patients with diabetes and PAD was particularly effective in preventing cardiovascular events. In this study, 36% patient had hypertension and treated to the same. In diabetic foot with PAD, the ankle-systolic blood pressure is less than the brachial systolic blood pressure, and the ABI is reduced to <1.00; PAD is defined as an ABI <0.90. Lower ABI values indicate more severe PAD and a higher risk of cardiovascular events. In the primary care setting, Mohler *et al.*<sup>16</sup> assessed perceptions of the ABI among 886 clinicians; most believed the ABI was useful in the diagnosis of both symptomatic (96%) and asymptomatic (89%) PAD. The ADA consensus statement recommends that a screening ABI is performed in all diabetic individuals more than

50 years of age. If normal (0.91-1.40), the test should be repeated every 5 years. Ankle-brachial pressure index is less useful in diagnosing PAOD as ABI may be normal or even more than normal in vessels which are calcified. As many patients in diabetic foot have calcified vessels. Palumbo and Melton<sup>17</sup> suggested X-ray of the extremities will identify calcified arteries that may be associated with high ABI levels, indicating non-compressible arteries. Toe-systolic blood pressure index may be helpful in identifying occlusive lower-extremity arterial disease in this circumstance. In this study, among the 14 patients, who underwent amputation with diffuse arteriosclerosis, 5 patients had normal ABI. All these 5 patients had very low TBI suggesting TBI is a better indicator of amputation in diabetic foot patient according to the study. In experienced hands, duplex scanning is as accurate as angiography and has the advantages of cost-effectiveness and safety. However, the aortoiliac segment can be difficult to visualize particularly in obese patients. For those patients in whom revascularization is considered and anatomical localization of stenoses or occlusions is important, an evaluation with a computed tomography angiogram or a magnetic resonance angiogram (MRA) may be valuable. Duplex ultrasound can directly visualize vessels and is also useful in the surveillance of post procedure patients for graft or stent patency. MRA is non-invasive with less risk of renal insult. It may give images that are comparable with conventional angiography, especially in occult pedal vessels, and may be used for anatomical diagnosis. In this study, four patients had arterial occlusion/stenosis at the level of the popliteal artery.

## CONCLUSION

Optimal ulcer healing requires adequate tissue perfusion. Thus, arterial insufficiency should be suspected if an ulcer fails to heal. Toe-brachial pressure index is a better index to diagnosis PAOD in diabetic ulcer foot patient, compared to ABI.

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# Serum Lactic Acid Levels, Lactate Clearance, and Uric Acid Levels as Prognostic Markers in Acute Coronary Syndrome Patients

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## Abstract

**Introduction:** India represents the highest burden of acute coronary syndrome (ACS) in the world. There is a rising trend in the development of coronary heart disease in the rural as well as urban India and two-fold increases in mortality from 1985 to present. We need to bridge the gap between available diagnostic facilities and treatment modalities among health-care practitioners.

**Aim:** The aim of this work was to assess the prognostic role of serum lactic acid, lactate clearance, and serum uric acid in ACS patients.

**Materials and Methods:** It is a prospective observational study. 50 patients admitted to our hospital intensive care unit with a diagnosis of ACS were included in our study.

**Sample Collection:** About 3 ml of venous blood is collected on admission and 48 h after admission. Serum lactic acid levels were estimated on admission and 48 h after in 50 patients and uric acid levels were tested on admission. The outcome of the patients, death or survival of the patient is recorded. Age, gender, body mass index, vital parameters, supportive measures given, electrocardiogram and Echo findings, blood urea and creatinine values, duration of hospital stay of the patient, and time of death since admission were noted. We also have compared the lactic acid levels, lactate clearance and uric acid levels with GRACE scoring system and Killip class.

**Results:** In our study, average uric acid levels were higher among survivors compared to nonsurvivors ( $P = 0.0019$ ). Serum uric acid levels were higher among patients with higher Killip class.

**Conclusion:** There is no significant difference in lactic acid levels between survivors and nonsurvivors ( $P = 0.83$ ). Lactic acid is positively correlated with GRACE score. Lactate clearance is negatively correlated with GRACE score.

**Key words:** Acute coronary syndrome, Lactic acid, Lactate clearance, Prognosis, Uric acid

## INTRODUCTION

Acute coronary syndromes (ACS) – unstable angina (UA), non-ST-elevation myocardial infarction (MI), and ST-elevation MI – are conditions caused by coronary vessel obstruction and thrombotic occlusions from rupture or erosion of a plaque.

India represents the highest burden of ACS in the world. There is a rising trend in the development of coronary heart disease in the rural as well as urban India and two-fold increases in mortality from 1985 to present. We need to bridge the gap between available diagnostic facilities and treatment modalities among health-care practitioners.

Following MI some proteins and enzymes labeled as cardiac markers (CK, MB/Troponin T and I) are released into the blood in large quantity from the necrotic heart muscle. These markers, CK-MB, Troponin-T, Troponin-I, and myoglobin have specific temporal profile in relation to MI; however, they do not correlate with myocardial function epidemiological studies have recently shown that lactic acid and a uric acid level are recognized as a gauge of metabolic

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function and have a diagnostic and/or prognostic role in different clinical settings.<sup>1</sup>

While the negative prognostic role of hyperlactatemia in several critical ill diseases is well established,<sup>2,3</sup> data in patients with acute cardiac conditions (i.e., acute myocardial ischemia) are scarce and controversial.<sup>4,5</sup>

Uric acid may be a risk factor for cardiovascular diseases and a prognostic marker for mortality in subjects with pre-existing heart failure.<sup>6-9</sup>

This study is aimed at summarizing available evidence on the clinical role of LA levels, lactate clearance and uric acid levels in ACS, focusing on its prognostic role.

## MATERIALS AND METHODS

### Study Design

Prospective observational study.

### Study Population

A total of 50 patients admitted to our hospital intensive care unit (ICU) with diagnosis of ACS were included in our study. 27 patients with inferior wall MI and 23 with anterior wall MI were included in our study group.

### Inclusion Criteria

Only those with electrocardiogram (ECG) evidence of MI or biochemical evidence of ACS.

### Exclusion Criteria

Those with known history of liver disease, renal disease, recent history of epileptic seizure, and sepsis was excluded.

### Duration of Study

2 months, July-August 2014.

### Sample Collection

About 3 ml of venous blood is collected on admission and 48 h after admission, serum lactic acid levels were estimated on admission and 48 h after and uric acid levels were tested on admission.

The outcome of the patients, death or survival of the patient is recorded. Age, gender, body mass index, vital parameters, supportive measures given, ECG and Echo findings, blood urea and creatinine values, duration of hospital stay of the patient, time of death since admission were noted and compared with serum levels of lactic acid and uric acid. We also have compared the lactic acid levels, lactate clearance, and uric acid levels with GRACE scoring system which is done for assessing 6 months mortality.

Uric acid levels were compared also with Killip class to check whether it is correlated with severity of the disease.

### Biochemical Markers

Lactic acid was estimated using semi auto analyzer kit method. Serum uric acid will be estimated by uricase method. Lactate clearance was calculated using the formula:<sup>10-12</sup>

$$\text{Lactate}_{\text{initial}} - \text{Lactate}_{\text{delayed}} / \text{Lactate}_{\text{initial}} \times 100\%$$

## RESULTS

Results were analyzed using Excel. Out of 50 patients studied 4 died. Since the sample size in the mortality group is less, we have correlated the serum lactic acid and uric acid levels with Grace scoring system using Pearson's correlation analysis. We have also correlated the uric acid levels with Killip class.

Since the non-survivor group is less, we have correlated lactic acid levels and lactate clearance with GRACE scoring system to assess whether it is associated with severity (Table 1).

GRACE scoring system is used to assess heart attack risk and guiding treatment. The Table 2 shows the 6 monthly mortality prediction of patients using GRACE scoring system.

Even though there is no significant difference in lactic acid levels between survivors and non-survivors, lactic acid and uric acid levels are well correlated with GRACE scores with significant *P* values (Table 3).

**Table 1: Baseline characters between survivors and non survivors**

Demographic characters	Survivors (n=46)	Non survivors (n=4)	P value (2-tailed t-test)	Statistically significant
Age (average±SD)	48.82±11.06	69.75±2.06	0.0005	Yes
Lactic acid	55.21, 14.19	56.75, 14.26	0.8360	No
Uric acid	5.404, 1.26	7.5, 0.25	0.0019	Yes
GRACE score	96.41, 20.4	176.75, 30.09	0.0001	Yes
Average hospital stay	7.23, 1.8	7, 1.41	0.8051	No
BMI	26.99, 3.88	29.915, 5.81	0.1707	No

SD: Standard deviation, BMI: Body mass index

We have compared lactate clearance with duration of ICU stay and Killip class.

Killip classification is used to stratify patients with MI and it focuses on physical examination and the development of heart failure to predict risk. Patients with higher Killip class have a higher frequency to die within the first 30 days.

This Figure 1 shows that decreased lactate clearance is associated with increased duration of ICU stay.

From the Figure 2, we can infer that decreased lactate clearance is associated with higher Killip class.

Table 4 indicates that patients with higher Killip class had higher serum uric acid levels.

This Figure 3 shows that average uric acid levels are higher in patients with increased duration of ICU stay.

## DISCUSSION

In this study, the venous lactate level immediately after admission with chest pain has been highly useful for the diagnosis of acute MI which is in concordance the study stating that lactic acid on presentation is highly sensitive for the diagnosis of MI.<sup>13</sup>

**Table 2: 6 months mortality prediction of study population using GRACE score value**

Risk category	GRACE risk score	Study group
Low	<86	13
Intermediate	86-120	27
High	>120	10* (4)*

\*In hospital mortality

**Table 3: Correlation of uric acid and lactic acid with GRACE score**

Variable	Correlation coefficient	P value	Significant?
Uric acid with GRACE score	0.335891348	0.01694	Yes $P < 0.05$
Lactic acid with GRACE score	0.321711846	0.022541	Significant

**Table 4: The comparison of uric acid with Killip class**

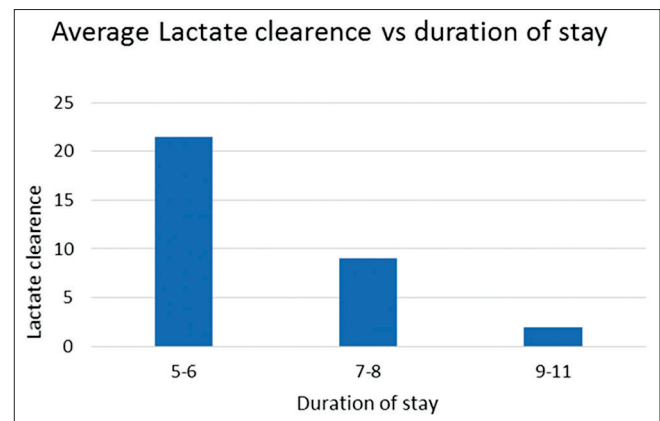
Killip class	<4	4-6	>6	Total
I	6	30	-	36
II	-	2	6	8
III	-	-	4	4
IV	-	-	4*	4*
Total	6	32	14	52

As observed serial lactate measurement or lactate clearance has been a prognostic tool for the duration of global tissue hypoxia (Trzeciak *et al.*).

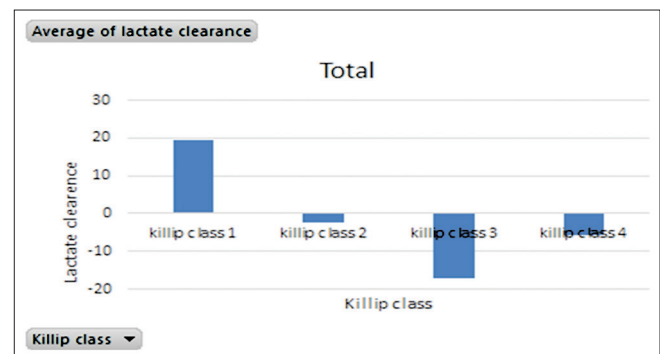
The study shows a close correlation between serum uric acid levels and Killip class in acute myocardial infarct patients in concordance with the study done recently in Japan (Japanese ACS study Kojima *et al.*).<sup>6</sup>

## CONCLUSION

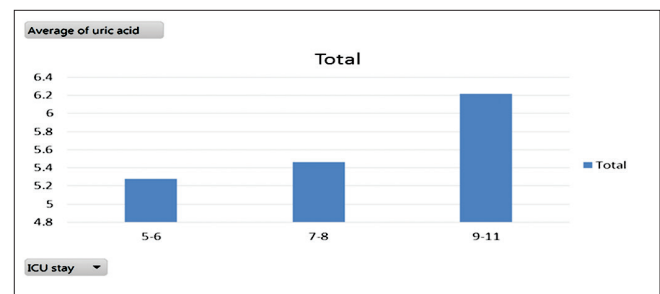
In our study, decreased lactate clearance and high uric acid levels were associated with increased risk of mortality. This



**Figure 1: Comparison of lactate clearance with duration of intensive care unit stay**



**Figure 2: Comparison of lactate clearance with Killip class**



**Figure 3: Comparison of uric acid with duration of intensive care unit stay**

study was done as a prospective observational study in a small number of patients. Larger studies are required to confirm our finding. This simple cost-effective test can guide therapy and assess the prognosis of MI patients in the near future.

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# Serum Uric Acid Level as an Independent Mortality Marker in Patients with Acute Myocardial Infarction

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## Abstract

**Background:** Hyperuricemia has been defined in patients who have congestive heart failure. Serum uric acid levels were noted in patients with acute MI and correlation with Killip's classification was studied and at the same time it was decided whether it affects mortality in such patients.

**Objective:** To study the relationship between serum uric acid level and mortality following acute myocardial infarction.

**Materials and Methods:** A total of 50 patients who were admitted and fulfilled the inclusion/exclusion criteria were evaluated by history, physical examination, electrocardiogram echocardiography, and serum uric acid levels.

**Result:** Out of 50 patients, 23 were females and 27 were males. 70% patients had ST-elevated myocardial infarction (STEMI), while 30% patients were of non-STEMI. In control group, 22 were females and 28 were males. The mean age of patients was 60.06 years with age ranging from 45 to 80 years. The mean age of the control group was 58.62 years with age ranging from 47 to 80 years. Standard deviation of test group was 7.70 while of control was 7.66, so test and controls were matching for age.

**Conclusion:** Serum uric acid levels are higher in patients of acute myocardial infarction as compared to normal healthy persons. Patients of higher Killip's class have higher uric acid levels. Patients who had myocardial infarction in past have higher serum uric acid and are in higher Killip's class.

**Key words:** Acute coronary syndromes, Cardiac failure, Killip's classification, Myocardial infarction, Serum uric acid

## INTRODUCTION

Acute coronary syndrome is composed of patients with,

1. Acute myocardial infarction with ST-segment elevation on their presenting electrocardiogram (ECG)
2. NSTEMI
3. Unstable angina.

ST segment elevation myocardial infarctions have been diagnosed on the basis of triad of:

1. Chest pain
2. Electrocardiographic changes
3. Elevated plasma enzyme activity.

Although acute myocardial infarction can occur without chest pain (20-25%) chest pain remains.

The most common symptom:

1. Chest pain  
Pain is the most common presenting complaint in patients with ST-segment elevation myocardial infarction. Pain is deep and visceral, adjectives commonly used to describe it are heavy, squeezing and crushing although occasionally described as stabbing and burning.
2. Electrocardiographic changes  
ECG is sensitive for detecting myocardial ischemia and infarction ECG criteria for diagnosis of ST

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segment myocardial infarction outlined in MILIS study are presence of any one of the following section.

- i. New or presumably new Q waves (at least 30 m wide and 0.20 mv deep) in at least
    - a. II, III or Avf
    - b. Leads v1 through v6 or
    - c. Leads I and Avl
  - ii. New or presumably new ST-T segment elevation or depression ( $>0.01$  mv measured 0.02s after J point in two contiguous leads of previously motioned lead combination or
  - iii. Complete left bundle branch block in appropriate clinical setting.
  - iv. The ECG diagnosis of right ventricular (RV) infarction offers special challenges, RV infarction occurs in the presence of inferior left ventricular infarction, and the resulting ST elevation is usually overwhelmed in the conventional precordial leads overlying the right ventricle (v2,v3) by the ST elevation in the opposing LV myocardium on the inferior surface. ST elevation must be sought in the right chest leads v1 and v3R through v6R, when found it provides reasonably strong evidence for the presence of RV infarction.
    - d. Posterior wall MI is indicated by ST-segment elevation in posterior leads v7-9.
3. Serum cardiac biomarkers:

Certain proteins called serum cardiac markers (CPK-MB/ Troponin-T and I) are released into the blood in large quantities from necrotic heart muscle agree myocardial infarction.<sup>1</sup>

Creatinine phosphokinase (CPK) rises within 4 to 8 h and returns to normal by 48-72 h. An important drawback of CPK measurement is a lack of specificity for ST-elevated myocardial infarction (STEMI) as it may be elevated in skeletal muscle trauma. It's MB enzyme is more specific. A ratio of creatine kinase-MB mass CK activity  $>2.5$  suggests but is not diagnostic of myocardial rather than a skeletal muscle source for the CKMB elevation.

Cardiac-specific Troponin T and I have amino acid sequence different from those of skeletal muscle forms of their proteins. Myoglobin is one of the first serum cardiac markers that rise above normal range after MI, it lacks cardiac specificity and is rapidly excreted in urine. Unstable Angina is defined as angina pectoris or equivalent Ischemic discomfort with at least one of three features:

1. It occurs at rest (or with minimal exertion) usually lasting  $>10$  min
2. It is severe and of new onset (i.e., within prior 4 to 6 weeks), and/or
3. It occurs with a crescendo pattern.

NSTEMI; diagnosis of NSTEM is established if a patient with clinical features of unstable angina develops evidence of myocardial necrosis as reflected in elevated cardiac biomarkers as described above.

The Killip's classification; Killip classified<sup>2</sup> patients with acute MI into 4 classes depending on the clinical manifestations of cardiac failure.

It is as follows:

- Class 1: No signs of pulmonary or venous congestion  
 Class 2: Moderate heart failure as evidenced by rales at lung bases, s3 gallap, tachypnea or signs of failure of right side of heart including venous and hepatic congestion  
 Class 3: Severe heart failure, pulmonary edema  
 Class 4: Shock with systolic pressure  $<90$  mmHg and evidence of peripheral venous constriction, peripheral cyanosis, mental confusion, and oliguria.

### Serum Uric Acid

It reflects circulating xanthine oxidase activity and oxidative stress production. Hyperuricemia has been defined in patients who have congestive heart failure. Serum uric acid levels were noted in patients with acute MI and correlation with Killip's classification was studied, and at the same time, it was decided whether it affects mortality in such patients.<sup>3-15</sup>

### Aims and Objectives

1. To note the Killip's classification of patients with acute myocardial infarction
2. To note the level of serum uric acid in patients of acute myocardial infarction
3. To correlate serum uric acid level with age, sex, body, mass index, diabetes mellitus, hypertension, past history of Ischemic heart disease, serum triglycerides
4. To correlate serum uric acid level with the Killip's classification
5. To note any relationship between serum uric acid level and mortality following acute myocardial infarction
6. To compare serum uric acid levels of patients with age and sex-matched healthy controls.

## MATERIALS AND METHODS

About 50 patients of acute MI who fulfill inclusion/exclusion criteria presented in 24 h onset of symptoms were studied. A detailed history and examination were carried out. All patients underwent routine investigations including hemoglobin, complete blood count, renal and liver function test, ECG, serum uric acid, serum triglycerides.

Patients were started on the treatment as per the attending physician. Patients were followed up till hospital stay.

About 50 age/sex matched normal healthy adults were also evaluated. People who had come for health check-up in OPD were studied for the same purpose.

### Inclusion Criteria

Any adult (>18 years) patients who were diagnosed as a case of acute MI (NSTEMI, STEMI) on the basis of clinical history, examination, biochemical markers, and admitted to emergency medical services/intensive care unit/medical wards of a tertiary care teaching hospital.

### Exclusion Criteria

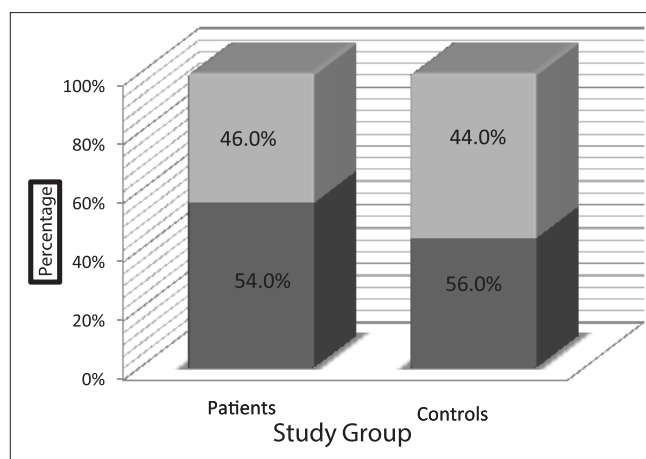
- a. Age <18 years
- b. Any patients who are a known case of:
  - i. Chronic renal failure/end stage renal disease
  - ii. Hyperuricemia/gout
  - iii. Hematological malignancy
  - iv. Hypothyroidism
  - v. Hyperparathyroidism
  - vi. Down's syndrome
  - vii. Bartter's syndrome
  - viii. Polycystic kidney disease
  - ix. Toxemia of pregnancy
  - x. Lead intoxication
  - xi. Sarcoidosis
  - xii. Berylliosis
  - xiii. Paget's disease
  - xiv. Patients in diabetic ketoacidosis
  - xv. H/O recent muscle injury/trauma
- c. Patients on drugs which increase serum uric acid
  - i. Salicylates (>2 g/day)
  - ii. Nicotinic acid
  - iii. Diuretics
  - iv. Ethambutol
  - v. Alcohol
  - vi. Pyrazinamide
  - vii. Levodopa
  - viii. Cyclosporine

From Table 1, it can be said that there is no significant difference as far as the sex ratio between the two groups is concerned.

Graph 1 shows that there was no significant difference in the sex ratio between the two study groups.

From Table 2, it can be said that there is no significant difference as far as the smoking status between the two groups.

From Table 3, it can be said that there is no significant difference in the diabetes status between the two groups.



Graph 1: Distribution of study group as per sex

Table 1: Association among study group between sex

St Group	Sex		Total	
	Male	Female		
Patients				
Count (%)	27 (54.0)	23 (46.0)	50 (100.0)	
Controls				
Count (%)	28 (56.0)	22 (44.0)	50 (100.0)	
Total				
Count (%)	55 (55.0)	45 (45.0)	100 (100.0)	
Chi-square test	Value	DF	P	Association is
Pearson Chi-square	0.040	1	0.841	Not significant
Fisher's exact test			1.000	Not significant

Table 2: Association among study group between, St. Group\*smoking

St Group	Smoking		Total	
	Yes	No		
Patients				
Count (%)	27 (54.0)	23 (46.0)	50 (100.0)	
Controls				
Count (%)	23 (46.0)	27 (54.0)	50 (100.0)	
Total				
Count (%)	55 (50.0)	45 (50.0)	100 (100.0)	
<b>Chi-square test</b>				
	<b>Value</b>	<b>DF</b>	<b>P</b>	<b>Association is</b>
Pearson Chi-square	0.640	1	0.424	Not significant
Fisher's exact test			0.549	Not significant

Graph 2 shows the ratio of diabetics and non-diabetics in both the study groups.

From Table 4, it can be said that there is no significant difference in hypertension between the two groups.

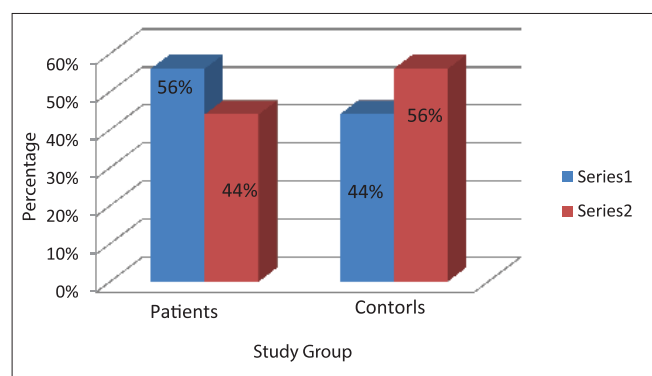
Graph 3 shows the ratio of hypertensive and non-hypertensive in both the study groups.

In Table 5 as  $P = 0.214$ , it can be said that there is no significant difference in both the groups far as age is concerned.

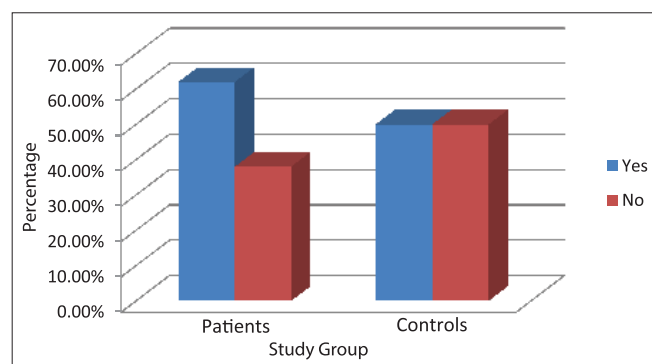
Hence, according to Table 6 and Mann-Whitney test, it can be said that there is a significant difference in uric acid levels between patients group. Thus, the patients with acute myocardial infarction have higher uric acid levels when compared with controls.

From the above Graph 4, it can be said that the serum uric acid levels in patients were higher (4.9) when compared to that of the controls (3.7).

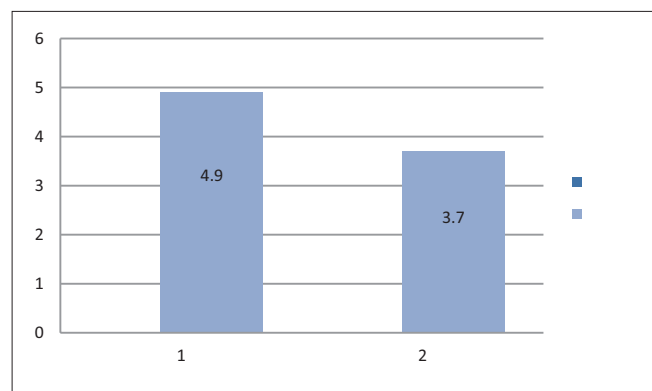
From Table 7, it can be said that there is no significant difference in uric acid levels in patients when compared on the basis of sex.



Graph 2: Comparison of DM among study groups



Graph 3: Comparison of DM among study



Graph 4: Comparison of Uric acid among study groups

From Table 8, it can be said that there is no significant difference in uric acid levels in patients when compared on the basis of sex.

Graph 5 shows serum uric acid level in both the study groups for both the sexes. It can be seen that there is no

Table 3: Association among study group between, St. Group\*DM

St Group	DM		Total
	Yes	No	
Patients			
Count (%)	28 (56.0)	22 (44.0)	50 (100.0)
Controls			
Count (%)	22 (44.0)	28 (56.0)	50 (100.0)
Total			
Count (%)	50 (50.0)	50 (50.0)	100 (100.0)
Chi-square test	Value	DF	P
Pearson Chi-square	1.440	1	0.230
Fisher's exact test			0.317
Association is			Not significant

Table 4: Association among study group between, St. Group\*HTN

St Group	HTN		Total
	Yes	No	
Patients			
Count (%)	31 (62.0)	19 (38.0)	50 (100.0)
Controls			
Count (%)	25 (50.0)	25 (50.0)	50 (100.0)
Total			
Count (%)	56 (56.0)	44 (44.0)	100 (100.0)
Chi-square test	Value	DF	P
Pearson Chi-square	1.461	1	0.227
Fisher's exact test			0.314
Association is			Not significant

Table 5: Comparison among study group for age

Age	n	Mean±SD	Median	IQR	Mann-Whitney Test	P
Patients	50	60.06±7.70	59.00	9.00	1.243	0.214
Controls	50	58.62±7.66	58.00	10.00	Difference is not significant	

Table 6: Comparison among study group for, uric acid

Uric acid	n	Mean±SD	Median	IQR	Mann-Whitney Test	P
Patients	50	5.25±1.17	4.90	0.90	7.846	4.31E-15
Controls	50	3.72±0.60	3.70	0.80	Difference is not significant	

Table 7: Comparison of uric acid level among patient group

Uric acid	n	Mean±SD	Median	IQR	Mann-Whitney test	P
Male	27	5.3±1.5	5.0	0.8	0.108	0.914
Female	23	5.2±0.6	4.9	0.9	Difference is not significant	

significant difference in both the groups as far as sex is concerned although the average is higher in the patient group.

Thus, Table 9 shows that there is no significant correlation between serum uric acid levels and age group, total cholesterol, total triglycerides, and body mass index in the patient group.

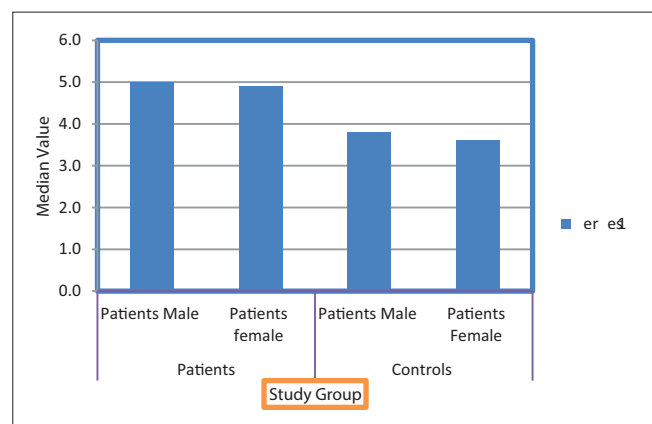
Thus, Table 10 shows that there is no significant correlation between serum uric acid levels and age group, total cholesterol, total triglycerides, and body mass index in the patient group.

Thus, Table 11 shows that there is no significant correlation between serum uric acid levels and the status of diabetes mellitus status.

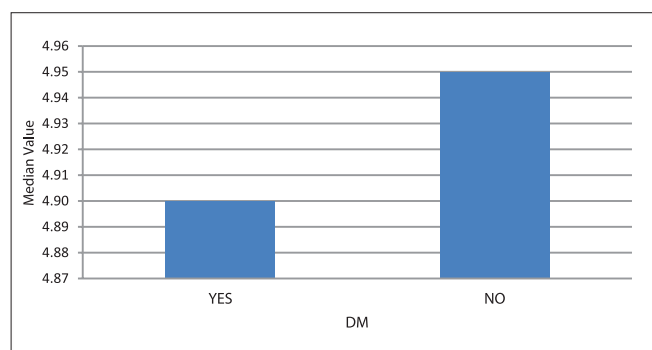
Graph 6 compares the serum uric acid levels among diabetics and non-diabetics,

Thus, Table 12 shows that there is no significant correlation between serum uric acid levels and the status of hypertension in the patient group.

Graph 7 compares the serum uric acid levels among hypertensive and hypertensives,



Graph 5: Comparison of uric acid among study groups



Graph 6: Comparison of uric acid among diabetic groups

Thus, Table 13 shows that there is a significant correlation between serum uric acid levels and past history of ischemic heart disease in the patients.

From the Graph 8, it can be seen that the serum uric acid levels in patients with past history of ischemic heart disease were significantly higher when compared to those with no history of ischemic heart disease.

Thus, Table 14 shows that as the Killip's class goes on increasing it has a significant correlation with the serum uric acid levels of the patients.

Graph 9 shows that as the Killip's class goes on increasing so does the serum uric acid levels, there being a significant correlation between the two.

Table 8: Comparison of uric acid level among control group

Uric acid	n	Mean±SD	Median	IQR	Mann-Whitney Test	P
Male	28	3.8±0.6	3.8	0.7	Difference is not significant	0.499
Female	22	3.7±0.6	3.6	0.8		

Table 9: Correlation between uric acid level and various study parameters among patient group

Variable	n	Mean±SD	Pearson correlation	P	Correlation is
Uric acid	50	5.252±1.1664			
Age	50	60.06±7.699	-0.067	0.664	Not significant
CHOL	50	225.78±35.438	-0.012	0.935	Not significant
TG	50	153.94±32.639	0.041	0.780	Not significant
BMI	50	26.688±1.9637	-0.017	0.906	Not significant

BMI: Body, mass index

Table 10: Correlation between uric acid level and various study parameters among patient control group

Variable	n	Mean±SD	Pearson correlation	P	Correlation is
Uric acid	50	3.722±0.6028	-0.051	0.724	Not significant
Age	50	58.62±7.664	-0.152	0.292	Not significant
CHOL	50	235.40±28.338	-0.231	0.106	Not significant
TG	50	138.38±34.467	-0.110	0.447	Not significant
BMI	50	25.126±3.0139			

Table 11: Comparison of uric acid level among patients with St Group=Patients

DM	n	Mean±SD	Median	IQR	Mann-Whitney test	P
Yes	28	5.35±1.46	4.90	0.90	307	0.992
No	22	5.13±0.64	4.95	0.80	Difference is not significant	

Thus, Table 15 shows that is a significant correlation between serum uric acid levels in patients who survived and those who died.

From Graph 10, it can be seen that the serum uric acid levels were higher in patients when compared to those who survived.

## DISCUSSION

The previous study has shown that serum uric acid increases in cardiac failure. Killip's classification denotes severity of cardiac failure in myocardial infarction. In a study done in Japan in 2005 by Kojima *et al.*,<sup>16</sup> it was shown that serum uric acid levels correlate with Killip's classification. Combination of Killip's class and serum uric acid levels after acute myocardial infarction is a good predictor of mortality in patients who have acute myocardial infarction. Using this study as referral study, we tried to study the correlation between serum uric acid and Killip's class and their prognostic value in our patients.

This study was conducted in 50 patients of myocardial infarction, who presented to the hospital within 24 h of the onset symptoms; 50 normal healthy controls of age and sex matching were also evaluated.

**Table 12: Comparison of uric acid level among patients with, HTN**

HTN	n	Mean±SD	Median	IQR	Mann-Whitney test	P
Yes	31	5.30±1.40	4.90	0.80	269	0.616
No	19	5.17±0.64	4.90	0.90	Difference is not significant	

**Table 13: Comparison of uric acid level among patients with, IHD**

IHD	n	Mean±SD	Median	IQR	Mann-Whitney test	P
Yes	12	6.15±1.93	5.75	1.05	92.5	0.002
No	38	4.97±0.39	4.90	0.50	Difference is significant	

**Table 14: Kruskal Walls one way analysis**

K-class	n	Mean±SD	Median	IQR	Kruskal-Wallis one way analysis	P
1.00	20	4.78±0.52	4.80	0.60	Chi-square	
2.00	15	5.01±0.32	4.90	0.50	17.28	<0.001
3.00	9	5.73±0.73	5.70	0.60	Difference is	
4.00	6	6.72±2.66	5.85	1.00	significant	

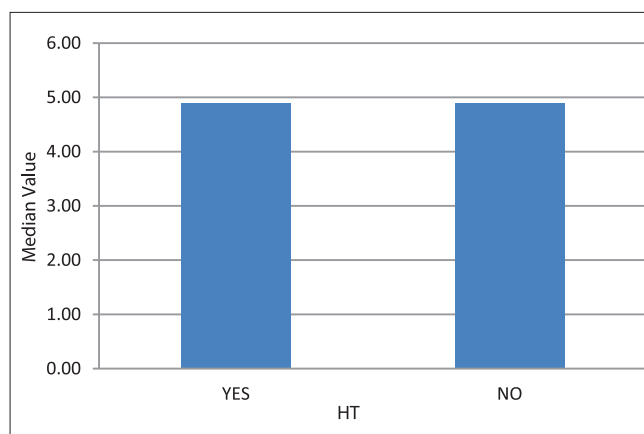
**Table 15: Outcome**

Outcome	n	Mean±SD	Median	IQR	Mann-Whitney test	P
Death	3	8.17±3.33	6.50	6.00	3.5	0.006
Survive	47	5.07±0.61	4.90	0.80	Difference is significant	

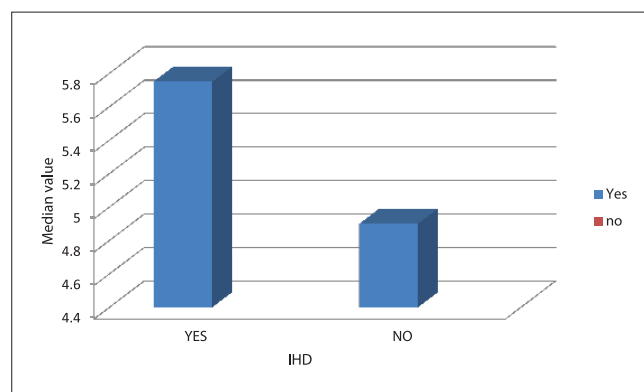
About 70% patients had STEMI, while 30% patients were of NSTEMI.

Blood samples for measurements of serum uric acid and other biochemical assessments were obtained immediately after admission. In controls, all the biochemical tests were done as a part of the health check-up plan.<sup>17-23</sup>

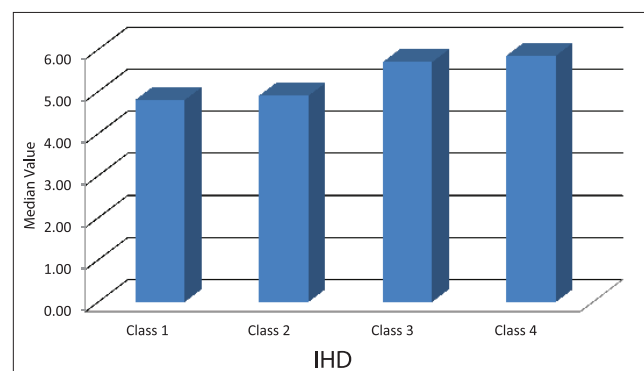
Uric acid concentration was expressed as mg per deciliter; uric acid was treated as a continuous variable and as a categorical variable and variables were divided into quartiles according to serum uric acid concentrations. The mean age



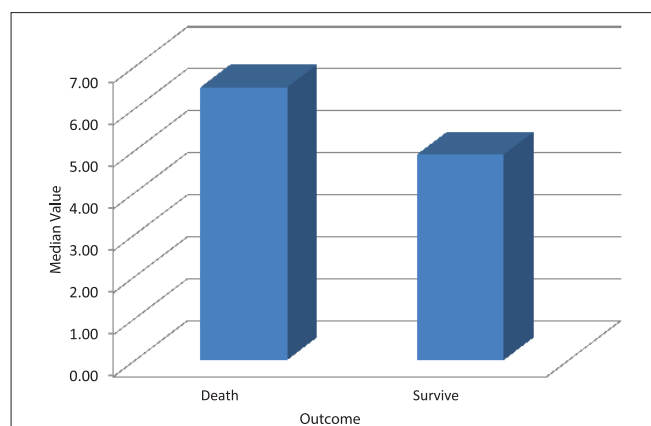
**Graph 7: Comparison of uric among HT groups**



**Graph 8: Comparison of uric acid among IHD groups**



**Graph 9: Comparison of uric acid among K class**



**Graph 10: Comparison of uric acid among patients who died and those survived**

of control group was 58.62 years with age ranging from 47 to 80 years.

Standard deviation of test group was 7.70 while of control was 7.66, so test and controls were matching for age.

Out of 50 patients, 23 were females and 27 were males. In control group, 22 were females and 28 were males.

A categorical variable and continuous variable.

Mean age of patients was 60.06 years with age ranging from 45-80 years.

Quantitative data is presented with the help of Mean, SD, Median and IQR. Comparison among study groups is done with the help of Mann-Whitney test and Kruskal-Wallis one-way analysis as per result of normality test.

Quantitative data are presented with the help of frequency and percentage table, the association among study groups is assessed with the help of Chi-square test.

$P < 0.05$  is taken as significant level.

Thus, the patients had higher serum uric acid levels probably because of acute myocardial infarction.

In referral study,<sup>16</sup> there were no controls. 1124 patients who presented with acute myocardial infarction within 48 hrs of onset of symptoms were evaluated and serum uric acid level at the time of admission was measured and correlated with Killip's class and other laboratory parameters.

$P = 0.644$  for correlation between serum uric acid and age. Hence, serum uric acid levels were not significantly associated with age of patients. In control group also there is no correlation between serum uric acid level and age. In study

population, there may not be a correlation between serum uric acid level and age for which further study needs to be done. This finding is different from study done by Conen *et al.* in 2004, Switzerland which showed serum uric acid levels were significantly associated but to a lesser degree with age.

There is no significant correlation between serum uric acid level n days of admission with sex of patients. Similarly, in control group also serum uric acid levels are not correlated with sex. While in referral study males had higher uric acid levels as compared to females.<sup>24,25</sup>

There was no significant correlation ( $P = 0.616$ ) between serum uric acid level and hypertension in patients. This is different from other studies<sup>16,23</sup> which show that hypertensive patients had hyperuricemia.

A total of 28 patients were known diabetics in the present study.  $P = 0.992$  for correlation between serum uric acid levels and diabetes (not significant). Hence, diabetic status was not significantly associated with serum uric acid levels. This finding is consistent with the study by Jakko *et al.* in which there was no significant association between serum uric acid levels and diabetic status. This finding is in contrast with other by Safi *et al.* which showed that Hyperuricemia is significantly associated with type 2 DM.

About 12 patients were known cases of ischemic heart disease p value was  $<0.005$  for correlation between serum uric acid levels and past history of ischemic heart disease. Hence, there is a significant correlation between serum uric acid level on the day of admission and history of ischemic heart disease. This finding is in confirmation with referral study.<sup>27</sup>

There is no significant correlation ( $P = 0.447$ ) between serum uric acid level on day of admission and body mass index. This finding is different from the previous studies<sup>27</sup> which showed that serum uric acid levels were significantly associated with components of metabolic syndrome, particularly obesity.

Total 3 patients expired. These patients are evaluated separately due to statistical reasons.

There is a correlation between serum uric acid level and Killip's class on day of admission. This finding is consistent with referral study.<sup>27</sup> Killip's classification is an indicator of severity of heart failure. The previous studies have shown that serum uric acid level increases in hear failure. So in this study serum, uric acid levels are indirectly correlated with severity of cardiac failure.

Thus there was a statistically significant correlation found between serum uric acid level and Killip's class. Patients

of Killip's class 3 and 4 had higher levels of uric acid as compared to patients of Class 1 and 2. This finding is consistent with referral study.<sup>27</sup>

Referral study had shown that there is a graded relation between serum uric acid concentration and creatinine concentrations in patients of acute myocardial infarction. In this study, there was no significant correlation between serum uric acid levels and creatinine concentration.

There is no significant correlation ( $R^2$  linear=0.001) between serum triglyceride level and serum uric acid concentration after acute myocardial infarction. This finding is inconsistent with Y Li *et al.* and one other study which showed serum uric acid levels were strongly associated with serum triglyceride levels.

Out of 50 patients 3 expired. They were in Killip's class 4 at the time of admission. Hence, higher Killip's class predicts poor prognosis. This result is similar to referral study. these patients had serum uric acid levels on the higher side. Therefore, it shows that serum uric acid is significantly correlated with Killip's class. However because of small number of patients statistical analysis could not be performed.

Thus overall from this study, it is concluded that combination of Killip's class and serum uric acid concentration is a good predictor of mortality in patients of acute myocardial infarction.

## CONCLUSION

1. Serum uric acid levels are higher in patients of acute myocardial infarction as compared to normal healthy persons.
2. Serum uric acid levels are correlated with Killip's classification. Patients of higher Killip's class have higher uric acid levels.
3. Serum uric acid levels and Killip's class are influenced significantly by previous myocardial infarction. Patients who had myocardial infarction in past have higher serum uric acid and are in higher Killip's class.
4. Serum uric acid and Killip's class independently and significantly predicted poor prognosis after acute myocardial infarction.
5. Combination of Killip's class and serum uric acid levels after myocardial infarction is a good predictor of mortality.
6. There is no correlation between serum uric acid level after acute myocardial infarction and age, sex, diabetic status, hypertension, body mass index, and serum triglyceride level.

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# Profile of Nonfatal Injuries in Road Traffic Accidents Cases Treated at a Tertiary Level Trauma Centre

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## Abstract

**Background:** Road traffic accidents (RTAs) are the major cause of preventable injury, consuming a large share of public health resources. A lack of trauma registry leads to ineffective predictive models.

**Aims and Objectives:** To study in detail parameters that describe nature and severity of injury along with demographic details for nonfatal RTA cases which can be used to develop the better prediction models to reduce morbidities and a more effective allocation of resources.

**Methods and Materials:** A retrospective study including all the nonfatal RTA cases presenting at our institute for 3 months duration, from January 2015 to March 2015. Information regarding name, age, gender, demography, time of occurrence, site of injury according to the injury severity score (ISS) mode of treatment given, clinical department which treated the patient, length of stay in hospital and the final outcome was recorded of all the eligible patients (1047). Patients were classified using ISS parameters.

**Results:** A total of 1047 patients were studied. A mean age was 34.4 years, 82% were males, maximum number of patients (28%) were young adults (20-29 years), head injury was present in more than half of the patients (575) followed by lower extremity (419), upper extremity (290), and face (250), 43% were admitted for indoor care, 52% of total admissions were in neurosurgery department and 37% were admitted in orthopedics, 45% of the admitted patients needed operative treatment, average length of stay was 8.7 days.

**Conclusions:** This study helped us in finding out certain characteristics which may be useful for planning preventive strategies and redirect public investment in preventive strategy and educational inputs for better safety measures.

**Key words:** Nonfatal road traffic accidents, Trauma registry, Epidemiology, Trauma prevention

## INTRODUCTION

According to the recent WHO report, trauma would become the third largest killer in developing countries by 2020.<sup>1,2</sup> About 20-50 million are injured every year in road

traffic accident (RTA) cases. Road crashes cost about USD \$518 billion globally. In India, RTAs and injuries account for 17% of disability-adjusted life years losses. It burdens the economy by 550 crores (12.5 billion dollars), an amount that is equal to our defense budget.<sup>3-7</sup>

When we look at the total burden of a busy trauma center, we can have an insight that majority of the cases which are nonfatal and can be diverted to the second level of care so that resuscitation facilities can be spared for more critical patients.

By doing this retrograde observational study, we want to derive exact data which can provide us useful information

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about the type, severity, nature, pattern of injury, and timings of RTAs. Simultaneously, we also want to study that with injuries related morbidity and its effect on the hospital stay and outcome of the patient.

Each region rather state has its peculiarities and behavior patterns which can affect nature of injuries. Even the economy and culture of the state can also affect driving pattern and traffic discipline.

Good quality, reliable, and representative information are a basis to make injury prevention programs. However, very little information is available from the centers that have been used many times in policy making.

Trauma registry is also very helpful in monitoring changing trends, identifying new problems, selecting interventions, and measuring the impact of interventions in an orderly timely manner.<sup>8</sup>

Hence, we decided to study the epidemiology and pattern of RTAs at our hospital.

## MATERIALS AND METHODS

A retrospective study was planned using medicolegal case records department as the source of all required information as all the RTA cases presenting to trauma center of this institute are recorded and treated as medicolegal cases.

For the purpose of the study, RTA was defined as “an accident which took place on the road between two or more objects, one of which must be any kind of moving the vehicle.”<sup>9</sup>

Data of all RTA cases presenting from January 2015 to March 2015 was analyzed with respect to name, age, gender, demography, time of occurrence, site of injury according to the injury severity score (ISS) mode of treatment received, clinical department which treated the patient, length of stay in hospital and the final outcome.

In accordance to the ISS, the body parts were divided into head, face, neck, thorax, abdomen, spine, upper extremity, and lower extremity for better understanding and comparability with other studies.

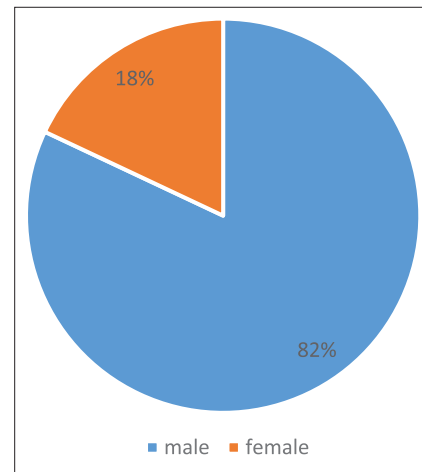
Cases with incomplete or incomprehensible records were filtered out.

The information we analyzed from this study was disseminated to promote the awareness and participation among the concerned professionals on various aspects of the RTAs.

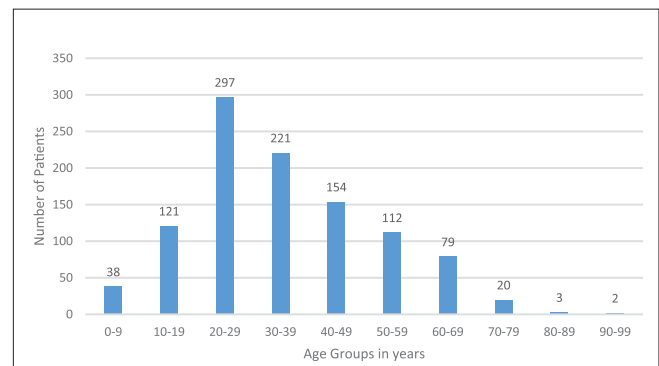
## RESULTS

The data collected from January 2015 to March 2015 showed a total of 1047 patients. Males (82%) were more commonly involved than females (18%) (Figure 1).

Mean age was 34.4 years, young adults (20-29 years) were found to be more commonly involved in accident cases (Figure 2).



**Figure1: Percentage distribution of Road Traffic Accident cases according to sex**



**Figure 2: Age distribution of road traffic accident cases**

Time most prone for accidents was 8:00 pm to 12:00 am midnight (Figure 3).

Head injury was the most common injury in RTA cases comprising more than 50% of the patients, followed by lower extremity, upper extremity and face in the decreasing order (Table 1).

About 43% of the RTA cases needed indoor care in various departments while 57% were treated on outdoor basis (Table 2).

Most of the indoor patients were admitted in neurosurgery (52%) and orthopedics (37%) department (Figure 4).

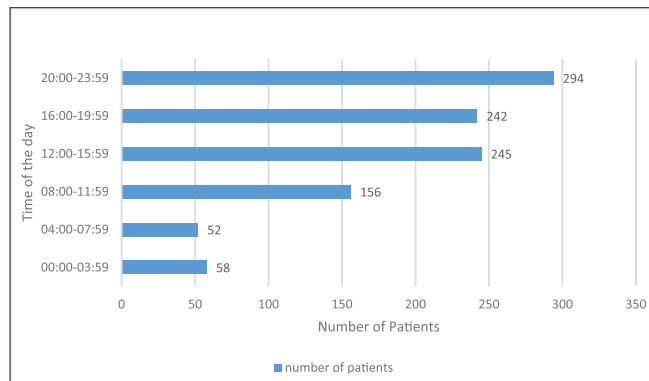
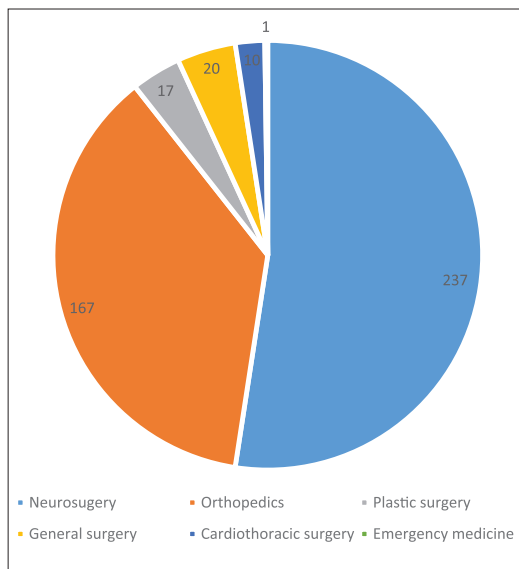
**Table 1: Involvement of body parts in the road traffic accidents**

Part of the body involved	Number of patients
Head	575
Face	250
Neck	11
Upper extremity	290
Spine	20
Thorax	36
Abdomen	36
Lower extremity	419
Perineum	1

**Table 2: Distribution of RTA cases on basis of indoor and outdoor care**

Total number of patients	1047
Indoor	452
Outdoor	595

RTA: Road traffic accident

**Figure 3: Time distribution of road traffic accident cases****Figure 4: Department wise distribution of admitted cases of road traffic accident cases**

About 45% of the admitted cases needed at least some kind of operative intervention (Table 3).

Around 20% of the patients admitted in neurosurgery needed operative intervention, while in orthopedics 80% of the patients were operated (Table 4).

The average duration of stay of indoor patients was 8.7 days.

## DISCUSSION

In India, just like in any other developing country, there has been an increase in motor vehicular accidents due to rapid urbanization and development of newer, faster, and heavier vehicles. This has resulted in increased amount of trauma. Our study provides comprehensive and useful insight into the epidemiology of trauma in Ahmadabad. Little literature is available for such issues in India, and a few international papers exist because of the difficulty in obtaining the reliable and detailed data and analyzing it.

Age group of 20-29 years was found to be the most commonly involved in RTAs highlighting the need for better safety education in this age group to reduce the incidence of RTAs. Other studies have found the similar outcomes 9, while some others found the age group of 25-34 to be the most common involved 4, this shows that the people in the most active and productive years of life are involved in RTAs, which amounts to a serious economic and emotional loss to their families and community as well. We found out that below and above the age of 20 and 49 years, the proportion of accidents was low. This may be because children are generally taken care of by elders and comparatively less use of vehicles in the adolescent age group. A lower incidence of RTAs in people aged 60 years and above may be due to generally less mobility of these people.

According to this study, accident rates were higher in males than in females in the ratio of 4.6:1, other studies also indicate the same 4, and there were 83% male and 17% female victims at JIPMER, Pondicherry.<sup>9</sup>

A number of accident cases was higher from 8:00 pm to 12:00 midnight due to increase in the traffic at this time compared to the rest of the day, indicating the need for better regulation of traffic in these hours. Late night accidents might be due to comparative less traffic leading to a tendency of over speeding by drivers and then leading to accidents. Hence, strict speed monitoring policies and educational policies should be implemented by the authorities.

**Table 3: Distribution of admitted cases according to mode of treatment (operative/conservative)**

Total admitted RTA cases	452
Conservative	248
Operative	204

RTA: Road traffic accident

**Table 4: Inter-departmental variation in mode of treatment of RTA cases**

Neurosurgery		Orthopedics	
Total patients 237		Total patients 167	
Operated	Conservatively managed	Operated	Conservatively managed
48	189	134	33

RTA: Road traffic accident

Head was the most commonly involved part of the body, highlighting the need for protective gear for head like helmets. Moreover, it again tells us to spread loud words of awareness for safety rules while driving.

Nearly 43% of the RTA cases needed admission highlighting the amount of burden RTA cases put on health resources of hospitals, further 45% of those admitted required some operative intervention.

Neurosurgery and orthopedic departments handled almost 90% of the RTA cases highlighting the need for better equipping and specialized training in these departments for more effective management of such cases. These departments require more manpower and skilled personnel to manage the workload.

The average duration of stay was found to be 8.7 days. For a tertiary care trauma center like us, the majority of patients are of poor or lower middle socioeconomic class, so these many days of loss of work, to the patient and the attendant creates additional burden on the family.

In our institute, only 20% of the patients admitted in neurosurgery needed operative intervention as we tend to have a low threshold for admission of patients with a head injury while in orthopedics 80% were treated operatively as only serious injuries requiring operation were mainly admitted while non-serious injuries were treated on outdoor basis. This highlights the need for distribution of resources accordingly.

In recent times, just like many other developing nations, road transport and health ministry of India are spending a lot of resources for developing trauma institutes, in such times, this kind of studies provide a very valuable source of information. Studies like this have been conducted in

some other cities such as Delhi, Mumbai, and Lucknow. They have helped dramatically in the development of more effective trauma centers.<sup>10</sup> There is a lack of accurate and uniform data in developing countries like India as trauma registry is in very primitive state as of now.

## CONCLUSION

The study of RTA cases at the emergency department of our hospital helped us find out some useful characteristics of this trauma epidemic, these characteristics may be useful for planning prevention strategies such as the development of protection mechanisms, stimulating the enforcement regarding the compliance of traffic rules by drivers and pedestrians, awareness of safety measures in an attempt to reduce the number and severity of accidents and redirect public investment in health for better facilities in trauma care.

In today's world of advanced technology, it is vital to set up trauma registry. Such registry is already available in high-income group countries while in low-income group countries trauma registry is virtually non-existent and in fact, more trauma victims are seen in these countries. A genuine initiative in this regard has been taken up by Government of India, Science and Technology Department in collaboration with Australian Government. Australia-India Trauma System collaboration-a research program has been started in 2014 at AIIMS, New Delhi, Sion Hospital, and Mumbai and at VS Hospital and NHL Medical College at Ahmedabad. A pilot project of trauma registry has been started in this year and once the results are verified, across the India in other major hospital trauma registry can be started which is very essential for optimum outcome in trauma cases. This will further reduce the load on economy by avoiding morbidity and dependency and wastage of resources.

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# Assessment of Biofilm Production in Clinically Significant Isolates of *Staphylococcus epidermidis* and Comparison of Qualitative and Quantitative Methods of Biofilm Production in a Tertiary Care Hospital

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## Abstract

**Introduction:** Coagulase-negative staphylococci (CONS) transformed from being commensals to pathogens causing a wide variety of infections. Meager nutritional requirements and ability to withstand various physical, chemical agents have made CONS a successful pathogen. Main virulence factor associated with CONS infections is biofilm formation. Biofilm helps CONS adhere to surfaces to escape the assault by immune mechanisms and antibiotics. The estimation of biofilm formation will help differentiate between commensal and pathogenic CONS.

**Purpose:** To determine clinically significant CONS and to ascertain their virulence using qualitative and quantitative methods of biofilm detection.

**Materials and Methods:** A total of 75 clinically significant isolates were taken up for the study. These isolates were segregated into two groups: Isolates with definite clinical significance (Group A - 45 isolates) and isolates with moderate significance (Group B - 30 isolates). Two qualitative methods Congo red agar method and tube method were employed. Quantitative detection of biofilm (adherence) was detected by microtiter plate (MTP) method.

**Results:** The more sensitive and quantitative method was MTP method. In Group A, 20 were moderate biofilm producers and 14 were strong biofilm producers. In Group B, 8 out of 30 were moderate biofilm producers and 6 were strong biofilm producers. The comparison of the three methods showed that MTP method was more sensitive in detecting of biofilm and helps in quantitative assessment on the amount of biofilm formation. Statistical significance of the difference between Group A and Group B isolates was found to be statistically significant,  $P = 0.004$ .

**Conclusion:** These methods are cost-effective and need minimal technical training. The detection of biofilm production will help differentiate pathogenic and commensal CONS. The reporting of biofilm will help the clinician to plan the appropriate line of therapy.

**Key words:** Adherence, Biofilm, Congo red agar, Microtiter plate method, *Staphylococcus epidermidis*, Tube method

## INTRODUCTION

Coagulase-negative staphylococci (CONS) are Gram-positive cocci living on each and every part of our body

and are seen abundantly in nature. As of now, 47 species and 23 subspecies have been identified.<sup>1</sup> This is excluding the animal pathogens and purely environmental organisms. These organisms are sturdy; they can live on meager nutrition, do not have specific growth requirements, grow well in a wide range of temperature and pH, and can form biofilms.<sup>2</sup> All these characteristics have given CONS the ability to thrive in varied circumstances. The mere number present on the skin in the presence of an ever growing population with waning immunity has given this organism a formidable stature. Modern medicine has grown by leap

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and bounds and so has the use of prosthetic devices. Here, the ability of biofilm formation gives CONS the survival advantage it needs to be a successful pathogen.<sup>3,4</sup> CONS are no more the commensals; they were thought to be in the early 1900's. Their presence in routine cultures can no more be discarded as improper sampling or contamination. Time is ripe to regard them as part of pathogens and proceed cautiously in the light of clinical correlation. The most common species implicated in human infections are *Staphylococcus epidermidis* and *Staphylococcus haemolyticus*. This is followed by other species such as *Staphylococcus saprophyticus*, *Staphylococcus lugdunensis*, *Staphylococcus hominis*, *Staphylococcus warneri*, *Staphylococcus cohnii*, *Staphylococcus simulans*, *Staphylococcus schleiferi*, *S. warneri*, and *Staphylococcus capitis*. Just like the established pathogen *Staphylococcus aureus* members of CONS are capable of causing a variety of infections. It can range from mild to moderate skin and soft tissue infections to limb and life-threatening infections such as bacteremia, native and prosthetic valve endocarditis, ophthalmic infections, prosthetic joint infections, and device-associated infection (cerebrospinal fluid [CSF] shunts, indwelling CSF catheters, intrathecal pumps, and ventriculostomy sites).<sup>5</sup> CONS-related urinary tract infections (UTIs) and catheter-related UTIs are on the rise. Among CONS, *S. saprophyticus* is strongly related to uncomplicated UTI in sexually active young females.

The property of adhesion by CONS was first observed by Bayston and Penny in 1972.<sup>6</sup> They observed mucoid colonies of CONS from CSF shunts. This was followed by many investigators using scanning electron microscopy on various prosthetic instruments and implants. These included critical devices such as peritoneal dialysis catheter,<sup>7</sup> intravascular catheters,<sup>8-10,11</sup> and pacemakers.<sup>12,13</sup>

Biofilms are composed of bacteria that stick to each other as well as to surfaces forming large communities. They produce an extracellular matrix comprising of polysaccharides and proteins.<sup>14</sup> The matrix allows the bacteria to stick to surfaces. The process of adhesion happens in a phased manner. Biofilms can be formed on biotic (like host tissue) or abiotic surfaces (like implants).<sup>4</sup> From here on the formation of biofilm happens in 4 steps. The initial attraction of bacteria toward a polymer surface can be due to hydrophobic interactions, van der Waal's forces, or surface charge.<sup>1</sup> Bacterium may also adhere via cell wall teichoic acids and proteins, such as autolysins or cell wall-associated proteins that interfere with collagen, fibronectin, or other matrix proteins. The bacteria quickly attach to biotic or abiotic surface. This is followed by rapid proliferation of bacteria and intracellular adhesion. Slowly, the biofilm matures into thick structured layer. This multilayered structure is well organized to have fluid filled cavities and channels. These channels play an important

role in supply of nutrition and the much required oxygen to the proliferating bacterial cells. *S. epidermidis*, which is the most common isolate member of the CONS family, produces polysaccharide intracellular adhesion (PIA). PIA comprises  $\beta$ -1, 6-linked glucose aminoglycan substituted with different side groups. Other factors that mediate biofilm are surface-associated proteins, accumulation-associated proteins (Aap), and biofilm-associated proteins (Bap/Bhp). CONS in a hospital environment or device-associated infections differ from the commensal CONS. Nosocomial CONS form thick multilayered biofilms on polymers or metals.<sup>3</sup>

The amount of biofilm production in CONS can help us assess the impact of CONS in relation to device-associated infections. Studies done in the past indicate that clinically significant bloodstream isolates of CONS produced slime.<sup>15-18</sup> Among the slime producers, *S. epidermidis* was the most prevalent species.<sup>16,19</sup> Nearly, 40-50% of CONS isolates from clinical specimens can be slime producers.<sup>19-22</sup> Bacterial films produced by a standard slime-producing strain of CONS on plastic tissue culture plates varied with the type of fixative.<sup>23</sup> The incidence of biofilm production by *S. saprophyticus* is comparatively less than *S. epidermidis*.<sup>24</sup> The percentage of slime-producing CONS ranged from 20% in the peritoneal fluid to 66% in CSF.

A number of simple and cost-effective tests are available to detect slime production by Staphylococci. The methods include microtiter plate (MTP) method,<sup>25</sup> tube method (TM),<sup>25</sup> Congo red agar (CRA),<sup>11,26</sup> bioluminescent assay,<sup>4</sup> and light or fluorescence<sup>27</sup> or confocal microscopic examination.<sup>9</sup> Marrie and Costerton have studied the biofilm formation using transmission electron microscopy in intravenous and intra-arterial catheters.<sup>28</sup>

Assessment of biofilm has been tried with different methods. The CRA method and TM are qualitative methods of assessment, whereas the MTP method is a quantitative method. TM helps in detection of strong biofilm producers. It is difficult to differentiate between moderate and weak biofilm producers using TM. The technically simple CRA method has very low level of correlation when compared with other methods. The sensitivity, specificity, and accuracy using the CRA method were elucidated in previous studies done by different researchers. The sensitivity, specificity, and accuracy were 7.6%, 97.2%, and 51.3%, respectively.<sup>29</sup> The TM, on the other hand, showed 77.9% sensitivity, 96% specificity, and 86.8% accuracy.<sup>25</sup> The qualitative method of biofilm estimation done by MTP method scored much better with a sensitivity of 96.2%, specificity of 94.5%, and accuracy of 97.3%.<sup>25</sup> The tissue culture plate or MTP method also has the advantage of being a quantitative model to study

biofilm formation by CONS on biomedical devices.<sup>29</sup> This study aimed at identifying the clinically significant *S. epidermidis* isolates and compares their ability to form biofilm using qualitative and quantitative methods.

## MATERIALS AND METHODS

The aim of the study was to determine the ability of CONS to form biofilms. This was done employing two different qualitative methods CRA method<sup>11</sup> and TM.<sup>25</sup> Quantitative detection of biofilm was detected using MTP method.<sup>25</sup>

This study was carried out in SRM Medical College Hospital and Research Centre, Kattankulathur, Kancheepuram District of Tamil Nadu. The study period was from April 2012 to March 2013. The study was carried out after obtaining the Institutional Ethics Committee approval. During the study period, 337 isolates of CONS were isolated from clinical samples. 262 samples which did not correlate with the clinical status of the patient were ruled out as contaminants/skin commensals. A total of 75 isolates were confirmed to be clinically significant isolates based on clinical and lab parameters. These isolates were segregated into two groups - isolates with definite clinical significance (Group A). The term definite significance was applied to those isolates which showed a clinical correlation in terms of signs of infection like fever and elevated white blood cell counts along with repeated isolation of the same organism. The comparison group was the isolates with moderate significance (Group B). Group B consisted of isolates which showed up on repeat cultures along with signs of infection like fever but did not show elevated white blood cell counts. Group A comprised 45 isolates of *S. epidermidis* and Group B comprised 30 isolates of *S. epidermidis* (Graph 1).

Modified CRA method - the test is based on the property of Congo red to stain polysaccharides black. If a given strain produces enough polysaccharide in the presence of Congo red in the medium, the colony formed will be black.<sup>26</sup> As a trial procedure to ascertain the percentage of various components that need to be added to the basal medium different concentrations of Agar (2%, 3%, 4%, and 6%) and varied concentrations of Congo red dye (0.2%, 0.4%, and 0.8%) were tried. 3% agar and 0.4% Congo red stain gave consistent results demarcating the biofilm producers and non-biofilm producers. In this study, we used trypticase soy broth as the basal media and added 5% sucrose, 3% agar, and 0.4% Congo red dye. The test samples were inoculated on the CRA plates and incubated aerobically for 24-48 h. The appearances of black-colored colonies were indicative of strong biofilm formation. Weak biofilm producers produced dark pink colonies. Non-biofilm

producers were seen as red, dry colonies.

TM - Test isolates were inoculated in trypticase soy broth and incubated overnight at 37°C. After incubation, the tubes were decanted and washed thrice with phosphate buffer saline (pH 7.3). The tubes were dried in air and stained with 0.1% crystal violet. After incubation for 10 min, the stain was decanted and washed with phosphate buffer saline. The tubes were dried in inverted position and observed for biofilm formation. Biofilm formation was considered positive when a visible film lined the wall and bottom of the tube. Tubes were examined and the amount of biofilm formation was scored as absent, weak, moderate, or strong. Ring formation at the liquid interface was not indicative of biofilm formation.

MTP method - Test isolates were inoculated in trypticase soy broth. The tubes were incubated overnight aerobically at 37°C. The broth culture was diluted 1:10 with freshly prepared trypticase soy broth. A 96 well MTP with flat bottom was used. First, three wells served as media controls without addition of cultures. 2 known in house positive and 2 negative controls were inoculated in each plate. The test organism diluted in trypticase soy broth was inoculated in triplicate and incubated overnight at 37°C aerobically. After 24 h of incubation on MTP, it was washed thrice with phosphate buffer saline to remove the free floating planktonic bacteria. 300 µl of methanol was added to each well and allowed to stand for 15 min. The excess of methanol was discarded and the wells of tissue culture plate were stained using 0.1% safranin stain. After 20 min of staining, the excess stain was discarded and washed with phosphate buffer saline. Finally, 33% glacial acetic acid was added to fix the stain. Optical density (OD) readings were determined using ELISA auto reader at a wavelength of 490 nm. The OD readings were considered as an index of bacteria adhering to the surface and forming biofilms.

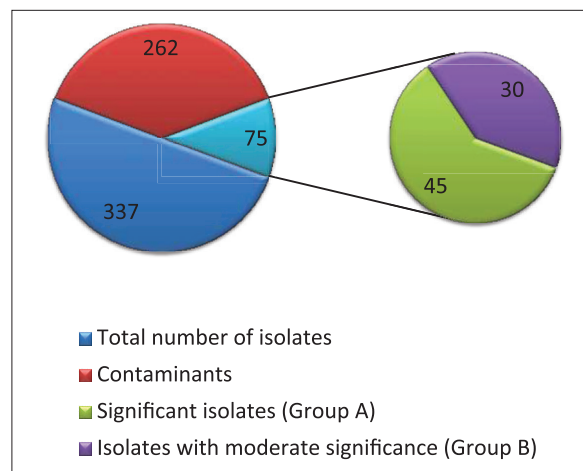
## RESULTS

Biofilm production by CONS was evaluated using three different methods: Modified CRA method, TM, and MTP method. Literature suggests the use of brain heart infusion agar with addition of 5% sucrose and 0.8% of Congo red dye. In the pilot study conducted, this combination did not work well and hence a modified method comprising of trypticase soy broth was tried instead of brain heart infusion agar. Various concentrations of Congo red dye (0.2%, 0.4%, and 0.8%), sucrose (2%, 4%, and 6%), and agar (2%, 3%, and 4%) were tried. The final combination of trypticase soy broth with 5% sucrose, 0.4% Congo red dye, and 3% agar gave satisfactory results. Group A showed 33 of 45 isolates of *S. epidermidis* to be non-biofilm

**Table 1: Comparison of biofilm detection using quantitative and qualitative methods**

Groups	CRA method (%)				TM (%)				MTP method (%)			
	Non-adherent	Weak	Moderate	Strong	Non-adherent	Weak	Moderate	Strong	Non-adherent	Weak	Moderate	Strong
Group A (n=45)	33 (73.3)	7 (15.5)	1 (2.2)	4 (8.9)	25 (55.5)	3 (6.7)	8 (17.8)	9 (20)	0 (0)	11 (24.4)	20 (44.4)	14 (31.1)
Group B (n=30)	21 (70.0)	5 (16.7)	0 (0)	4 (13.3)	10 (33.3)	4 (13.3)	10 (33.3)	6 (20.0)	0 (0)	16 (53.3)	8 (26.7)	6 (20.0)

CRA: Congo red agar, TM: Tube method, MTP: Microtiter plate



**Graph 1: Distribution of isolates of *Staphylococcus epidermidis* during study period**

producers. 7 out of 45 isolates were weak biofilm producers, 1 isolate of *S. epidermidis* was found to be moderate biofilm producer, and 4 out of 45 isolates of *S. epidermidis* were found to be strong biofilm producers producing jet black crystalline colonies. In Group B, 21 out of 30 isolates were non-biofilm producers, 5 out of 30 isolates showed weak biofilm formation, and 4 isolates showed strong biofilm formation. 0.1% crystal violet stain was used in TM for assessment of biofilm. In Group A, 25 out of 45 isolates of *S. epidermidis* were found to be non-adherent, 3 out of 45 isolates of *S. epidermidis* were weak biofilm producers, 8 out of 45 isolates of *S. epidermidis* were moderate biofilm producers, and 9 out of 45 isolates of *S. epidermidis* were strong biofilm producers. In Group B, 10 out of 30 isolates of *S. epidermidis* were non-adherent, 4 out of 30 isolates were weak biofilm producers, 10 out of 30 isolates of *S. epidermidis* were moderate biofilm producers, and 6 out of 30 isolates were strong biofilm producers. Both modified CRA method and TM failed to provide a quantitative analysis on biofilm production. The results of both these methods were prone to observer bias (Graph 2).

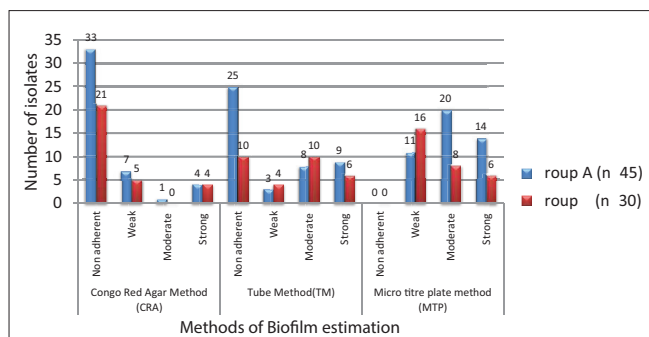
The more sensitive and quantitative method of estimation of biofilm production was by MTP method. Two dyes, 0.1% crystal violet, and 0.1% safranin were used for assessment of biofilm production. In our study, 0.1% safranin yielded better results. In Group A, 11 out of 45 isolates of

*S. epidermidis* were found to be weak biofilm producers, 20 were moderate biofilm producers, and 14 were strong biofilm producers (Figure 1). In Group B, 16 out of 30 isolates of *S. epidermidis* were weak biofilm producers, 8 out of 30 were moderate biofilm producers, and 6 were strong biofilm producers (Table 1). The comparison of the three methods showed that MTP method was more sensitive in detecting of biofilm and helps in quantitative assessment on the amount of biofilm formation.

Statistical significance of the difference between Group A and Group B isolates of *S. epidermidis* with reference to the degree of biofilm production was assessed using Chi-square test and were found to be statistically significant,  $P = 0.004$ .

## DISCUSSION

CONS are ubiquitous in nature. The mere presence in large numbers on the skin, minimal nutritional requirements coupled with very potent virulence factors such as biofilm formation provide a survival advantage to this organism. Technological innovations in the field of science have resulted in increased use of indwelling devices. This coupled with inadvertent use of antibiotics has helped this commensal become a potential pathogen. In the era of increasing immuno/immune compromised population and emerging and re-emerging infections, CONS have established itself as pathogenic bacteria. The dilemma exists in differentiating commensal CONS from the offending organism. Antibiotic resistance methicillin resistance CONS alone cannot be taken into account for differentiating commensal from pathogenic CONS as many of the commensal CONS exhibit resistance to cefoxitin. The cost-effective alternative available is the assessment of biofilm formation. Biofilm if present would mean that the antibiotics may not be fully effective as bacteria are not exposed to the action of antibiotic. The use of nucleic acid amplification techniques for detection of biofilm-associated genes are costly, cumbersome and need technical expertise which may not be available everywhere in resource-poor countries. Biofilm production is one of the major characters which help a commensal bacterium to become pathogenic under appropriate situations. Biofilms are communities of microorganisms that stick to each other or to the surfaces



Graph 2: Comparison of biofilm detection using quantitative and qualitative methods



Graph 3: Determination of biofilm production by *Staphylococcus epidermidis* isolates using safranin dye in microtiter plate method (quantitative method)

by the production of extracellular matrix comprising of polysaccharides and proteins. First, the bacterium attaches to surfaces by the use of non-specific factors such as hydrophobicity and surface charge. Bacterium may also adhere to surfaces via cell wall teichoic acids and proteins, such as autolysins or cell wall-associated proteins that interfere with collagen, fibronectin, or other matrix proteins. After this, initial phase of adherence comes the stage of actual biofilm formation where the bacteria produce factors helping in the cell-to-cell contact. The most commonly isolated CONS, *S. epidermidis* produces PIA. PIA comprises of  $\beta$ -1, 6-linked glucose aminoglycan substituted with different side groups. Other factors that mediate biofilm are surface-associated proteins, Aap, and Bap/Bhp. CONS in hospital environment or in device-associated infections differ from the commensal CONS. Nosocomial CONS form thick multilayered biofilms on polymers or metals.

Three methods of detection of biofilm, namely, the modified CRA method, TM, and MTP method were evaluated. Many authors have suggested brain heart infusion agar with addition of 5% sucrose and 0.8% of Congo red dye. However, this combination of brain heart

infusion agar, 5% sucrose, and 0.8% Congo red dye did not work well in our hands. An alternative method using trypticase soy broth was tried instead of brain heart infusion agar. Various concentrations of Congo red dye (0.2%, 0.4%, and 0.8%), sucrose (2%, 4%, and 6%), and agar (2%, 3%, and 4%) were tried. A combination of trypticase soy broth with 5% sucrose, 0.4% Congo red dye, and 3% agar gave satisfactory results.

The comparison of these three methods of biofilm production leads us to conclude that the biofilm detection by MTP method is more sensitive and also helps in qualitative assessment of biofilm formation. In our study, 30.4% of isolates causing infections were strong biofilm producers.

## CONCLUSION

The above-mentioned methods are cost-effective and need minimal training of laboratory staff and do not require any special instruments. The procedure can be carried out along with the routine bacteriological workup of a laboratory. The detection of biofilm production will be an added tool in the hands of a microbiologist to differentiate pathogenic and commensal CONS. The reporting of biofilm will help the clinician to plan the appropriate line of therapy. Routine reporting of biofilm will create an atmosphere where the microbiologist and clinician can join hands toward successful antibiotic stewardship.

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# Association of Dry Eyes with Connective Tissue Disorder

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## Abstract

**Introduction:** Dry eye, or Keratoconjunctivitis sicca, is a multifactorial condition that affects the tear film and ocular surface due to abnormalities in the quality or quantity of the tear film which is commonly observed in systemic autoimmune disorders. The early recognition of disease and treatment provides a better visual function.

**Aim:** To study the incidence and factors influencing the expression of dry eyes in connective tissue disorders.

**Material and Methods:** It is a prospective cohort study of 100 patients of connective tissue disorders conducted in Tirunelveli Medical College Hospital. In this study, Schirmer's test, tear meniscus height, tear break up time, fluorescein stain, and rose Bengal stain were used to diagnose and grade dry eyes.

**Results:** Among 100 patients, 11 were diabetics, in which 5 were diagnosed to have dry eyes (45.5%). Among affected males, 4 had smoking history (66.6%). Among those affected, mild dry eyes seen in 16 patients (44.44%), moderate dry eyes in 12 patients (33.3%), severe dry eyes seen in 8 patients (22.2%).

**Conclusion:** Comorbid conditions, like smoking, menstrual irregularities are directly related to the severity of dry eyes and should be treated simultaneously.

**Key words:** Connective tissue disease, Dry eye, Menopause, Smoking

## INTRODUCTION

Dry eye, or Keratoconjunctivitis sicca, is a multifactorial condition that affects the tear film and ocular surface due to abnormalities in the quality or quantity of the tear film. This condition is accompanied by an increase in the tear film's osmolarity and inflammation of the ocular surface. Dry eye is commonly observed in systemic autoimmune disorders such as rheumatoid arthritis (RA), systemic lupus erythematosus, and Sjögren's syndrome (SS) with a prevalence ranging from 14.5% to 56%. This condition is characterized by symptoms of ocular irritation and discomfort, which affect functional visual acuity and the ability to work, read, use a computer,

and drive at night.<sup>1</sup> The majority of patients with SS are women, and the diagnosis is usually done when they are 40-50-year-old.<sup>2</sup> The presence of associated with systemic diseases like diabetes mellitus greatly affects the tear film function and stability. Decreased Schirmer 1 test values and shorter break up time (BUT) were positively correlated with the subjective severity of dry eye symptoms in type 2 diabetic patients.<sup>3</sup> Tear production and stability, surface dryness, and inflammation were significantly related to hormonal fluctuations in the menstrual cycle. Any impairment in normal menstrual cycle increases symptoms of dry eyes.<sup>4</sup> Dry eye also increases the risk of eye infection and destruction of ocular tissue. Ocular symptoms are correlated to systemic disease activity and can present as an initial manifestation of connective tissue disorder. The early recognition of disease and treatment provides better visual function.

## Aim

To find the incidence of dry eyes in connective tissue disorders and factors associated with expression of dry eye symptoms and severity.

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## MATERIALS AND METHODS

A prospective cohort study was conducted in Department of Ophthalmology, Tirunelveli Medical College Hospital. Institutional Ethics Committee and informed consent from the study patients were obtained. Patients with connective tissue disorder were included in the study. In this study, Schirmer's test Types I and II, tear meniscus height, tear BUT (TBUT), fluorescein stain, and rose Bengal stain were used to diagnose and grade dry eyes. Its severity is classified into mild, moderate, severe, and very severe (level 1 to 4) according to DEWS dry eye grading system. Mild-dry-eyes are diagnosed by the presence of mild irritation, dryness with variable Schirmer's, and TBUT without any other abnormalities. Moderate-dry-eyes are diagnosed by Schirmer's  $\leq 10$ , TBUT  $\leq 10$  with a variable amount of corneal and conjunctival staining and visual symptoms. Severe-dry-eyes diagnosed by Schirmer's and TBUT of  $< 5$  with marked corneal and conjunctival staining, filamentary keratitis, mucus debris, and visual symptoms. Very-severe-dry-eyes diagnosed by disabling visual symptoms with Schirmer's  $< 2$ , TBUT - immediate dry spot, filamentary keratitis, ulceration, increased tear debris, and keratinization.

## RESULTS

A total of 100 patients with connective tissue disorder were included, 90 females, 10 males. Among 100 patients, 54 were diagnosed to have RA, 24 were diagnosed to have systemic lupus erythematosus, 22 diagnosed to have other kinds of connective tissue disorders like systemic sclerosis, scleroderma with interstitial lung disease. Among females 30 (33.3%) were diagnosed to have dry eyes, among males 6 (60%) were diagnosed to have dry eyes. 15 affected females were in perimenopausal age group (40-50 years) (50%). Next, a common age group affected in females were 51 to 60 years old (30%). 6 out of 30 affected females had menstrual irregularities (20%). Among 100 patients, 11 were diabetics, in which 5 were diagnosed to have dry eyes (45.5%). Among affected males, 4 had smoking history (66.6%). Among those affected, 18 patients had a history of steroid intake (32.5%). Among 36 patients, mild dry eyes are seen in 12 patients (33.3%). Moderate dry eyes are seen in 16 patients (44.44%). Severe dry eyes are seen in 8 patients (22.2%). Among 36 affected patients 12 had defective vision of which 6 had cataract changes, 4 had hypermetropia, and 2 had myopia. Among severe dry eye patients who were treated with 0.1% tacrolimus eye ointment 5 showed improvement (62.5%).

## DISCUSSION

In our study, female patients were enrolled in higher number which is comparable with Usuba *et al.* study.<sup>1</sup>

Menstrual irregularities are associated with more expression of dry eyes due to hormonal factors which are comparable with Versura *et al.* study<sup>4</sup> which shows ocular surface changes during the menstruation. RA is three times a more common in females than males in our study which have a positive correlation with Choudhary *et al.* study.<sup>5</sup> Peri- and post-menopausal females were commonly affected in our study which is similar to Wenderlein *et al.* study<sup>2</sup> which shows a direct correlation with dry eye phenomenon and estrogen function (Table 1).

Diabetes as a comorbid factor for dry eyes was found to be significant which is compared with Eissa *et al.* study<sup>3</sup> (Table 2).

Effect of smoking was found to be an important risk factor in dry eyes by retarding tear secretion which is similar to Uchino *et al.* study<sup>6</sup> (Table 3).

About 0.1% tacrolimus eye ointment used in our study for severe dry eyes improved tear stability and ocular surface status which is correlating with Moscovici *et al.* study.<sup>7</sup> Among 36 patients, 66.62% were diagnosed only at the stage of moderate to severe dry eyes.

## CONCLUSION

Secondary dry eye syndrome is a chronic multifactorial condition. Comorbid conditions, like diabetes, menstrual irregularities are directly related to the severity of dry eyes and should be treated simultaneously. Therapies are mainly aimed to improve symptoms and for maintenance of

**Table 1: Distribution dry eye in female patients**

Menopause	Dry eye	
	Yes	No
Premenopausal	6	31
Perimenopausal	15	16
Postmenopausal	9	13

**Table 2: Distribution of dry eye in diabetic patients**

Diabetic history	Dry eye	
	Yes	No
Diabetics	5	6
Nondiabetics	31	58

**Table 3: Distribution of dry eye in smoking history**

Smoking history	Dry eye	
	Yes	No
Smoker	4	2
Nonsmoker	2	2

visual function. Screening of all connective tissue disorder patients for dry eyes and early intervention is needed to provide a better visual prognosis.

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# Prevalence of Overweight and Obesity in Adolescent Children: A Cross-sectional Study

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## Abstract

**Introduction:** Obesity is the most prevalent form of nutritional disorder in many of the affluent countries. Obesity is a state of excess adipose tissue mass.

**Materials and Methods:** Secondary data analysis of a school-based cross-sectional study in a rural and urban school of Kochi city. Weight, height, sex, and age routinely recorded by health visitors. Height, weight, and body mass index (BMI) standardized for age and sex. SD score >1.04 for BMI (>85<sup>th</sup> centile) was defined as overweight and >1.64 (>95<sup>th</sup> centile) as obese.

**Results:** Out of the 254 girls of the rural school, 6 were obese (8.74%) and 25 were overweight (42.66%). Of these, obesity and overweight were more common among 12-year-old girls, 6.06% and 12.12%, respectively. Of the 220 girls of urban schools, 6 were obese (11.08%) and 21 were overweight (49.9%). Of these, obesity and overweight were more common in the 13 years old age group of 3 (5.56%) and 8 (14.81%), respectively. Of the 191 boys of the rural school, only 1 (1.27%) was obese and 12 (29.13%) were overweight. Of these, obesity and overweight were more in the 14 year age group of 1 (1.27%) and 4 (5.06%), respectively. Of the 272 boys of the urban school, 15 (21.91%) were obese and 38 (55.74%) were overweight. Of this, obesity was more among the 14-year-old children. Obesity in girls showed no statistical significance with the urban and rural population ( $P = 0.9, 64, 233$ ).

**Conclusions:** Obesity is a serious health issue, resulting in both mortality and morbidity. We need to promote early intervention programs which should be aimed at weight reduction. Parents and children must be counseled not to eat junk foods and carbonated drinks.

**Key words:** Adolescent, Obese, Overweight, Prevalence

## INTRODUCTION

Obesity is the most prevalent form of nutritional disorder in many of the affluent countries. Obesity is a state of excess adipose tissue mass. According to the WHO statistics, more than 1.6 billion people  $\geq 15$  year old are overweight or obese. As per various recent studies in India, 10-15% of school children are overweight. More than 66% of US adults are categorized as overweight or obese, and the prevalence of obesity is increasing rapidly in most of the industrialized world. Obesity is also associated with

an increased risk of multiple health problems, including hypertension, Type 2 diabetes, dyslipidemia, obstructive sleep apnoea, non-alcoholic fatty liver disease, degenerative joint disease, and some malignancies; childhood obesity is not only confined to industrialized countries. Therefore, a rational clinical approach needs to be applied to preventing and treating this disorder.<sup>1</sup>

Visceral adipose tissue is significantly related to concentrations of plasma low-density lipoprotein cholesterol and triglycerides in 11-15 year old as well as to concentrations of basal insulin and high-density lipoprotein cholesterol (inversely) in females aged 10-16 years.<sup>2,3</sup>

## MATERIALS AND METHODS

The study was a cross-sectional, randomized, epidemiological study among adolescent school students of the rural and

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urban school of a city in Kerala. A total number of 937 school children aged 12-15 years of both urban and rural school had participated in this study. Out of them, 445 were from the rural school, and 492 were from the urban school. The body weight was measured barefoot using a measuring scale and height to the nearest centimeter was taken. Body mass index (BMI) was calculated as weight (in kilograms) divided by height (in meter squared). For adolescent children, after BMI is calculated, the BMI number is plotted on the CDC BMI-for-age growth charts (4) (for either girls or boys) to obtain a percentile ranking. Percentiles are the most commonly used indicator to assess the size and growth patterns of individual children in the United States. Percentiles are used for adolescent because the amount of body fat differs between boys and girls and body fat also changes with age. The percentile indicates the relative position of the child's BMI number among adolescent children of the same sex and age. Healthy children have a BMI percentile ranging between 5<sup>th</sup> percentile and 85<sup>th</sup> percentile. The children whose weight were >85<sup>th</sup> to <95<sup>th</sup> percentile were considered as overweight and obese who were ≥95<sup>th</sup> percentile (WHO 2000).

Chi-square test was used to find out the significance. Odd's ratio indicates that there is a strong hazardous association between sex and obesity.

## RESULTS

Of the 254 girls of the rural school, 6 were Obese (8.74%) and 25 were overweight (42.66%). Of these, obesity and overweight were more common among 12-year-old girls, 6.06% and 12.12%, respectively (Table 1 and Figure 1).

Of the 220 girls of urban schools, 6 were obese (11.08%) and 21 were overweight (49.9%). Of these, obesity and overweight were more common in the 13 years old age group of 3 (5.56%) and 8 (14.81%), respectively (Table 2 and Figure 2).

Of the 191 boys of the rural school, only 1 (1.27%) was obese and 12 (29.13%) were overweight. Of these, obesity and overweight were more in the 14 year age group of 1 (1.27%) and 4 (5.06%), respectively (Table 3 and Figure 3).

Of the 272 boys of the urban school, 15 (21.91%) were obese and 38 (55.74%) were overweight. Of these, obesity was more among the 14-year-old children (Table 4 and Figure 4).

Obesity seems to be growing in children regardless of sex. In the USA, 16% of children and adolescent are obese

and 20% are overweight. 4% of adolescents have severe obesity. It can be noted that there is a sex-wise variation in the prevalence of overweight and obesity in children irrespective of the place as revealed in many studies done

**Table 1: The prevalence of obesity among girls of rural schools**

Group	Age	No	n (%)		
			Obese	Overweight	Normal and underweight
Rural girls	12	66	4 (6.06)	8 (12.12)	54 (81.82)
	13	20	0 (0)	2 (10)	18 (90)
	14	112	1 (0.89)	7 (6.25)	104 (92.86)
	15	56	1 (1.079)	8 (14.29)	47 (83.93)
Total		254	6 (8.74)	25 (42.66)	223 (87.8)

**Table 2: The prevalence of obesity among girls of urban schools**

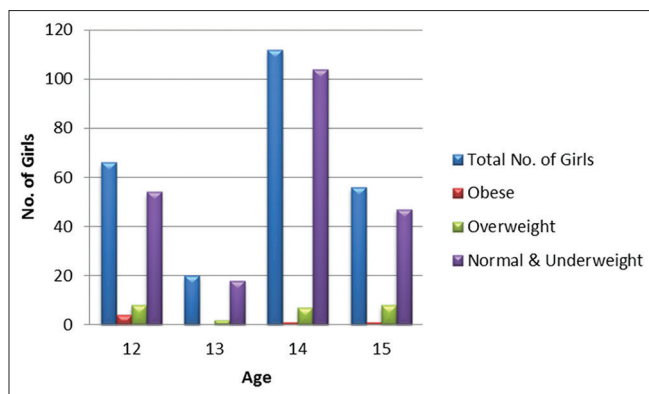
Group	Age	No	n (%)		
			Obese	Overweight	Normal and underweight
Urban girls	12	57	1 (1.75)	5 (8.77)	51 (89.47)
	13	54	3 (5.56)	8 (14.81)	43 (79.63)
	14	56	0 (0)	8 (14.29)	48 (85.71)
	15	53	2 (3.77)	0 (11.32)	51 (84.91)
Total		220	6 (11.08)	21 (49.19)	193 (87.73)

**Table 3: Comparison of obesity among rural and urban girls**

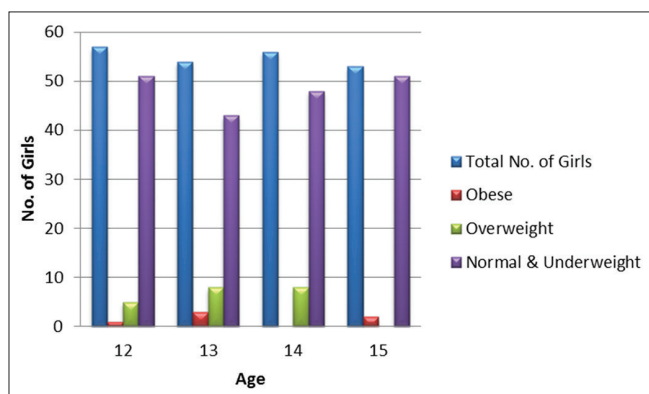
Locale	Obese	Overweight	Normal and underweight	Total
Girls				
Rural	6	25	223	254
Urban	6	21	193	220
Total	12	46	416	474
Expected				
Rural	6.43,03,797	24.6,49,789	222.91,98,312	254
Urban	5.56,96,203	21.3,50,211	193.08,01,688	220
Total	12	46	416	474
P	0.9,64,233			

**Table 4: The prevalence of obesity among boys of rural schools**

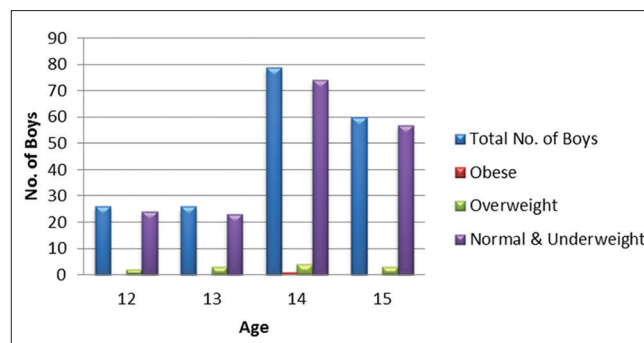
Group	Age	No	n (%)		
			Obese	Overweight	Normal and underweight
Rural boys	12	26	0 (0)	2 (7.69)	24 (92.31)
	13	26	0 (0)	3 (11.54)	23 (88.46)
	14	79	1 (1.27)	4 (5.06)	74 (93.67)
	15	60	0 (0)	3 (5)	57 (95)
Total		191	1 (1.27)	12 (29.3)	178 (93.2)



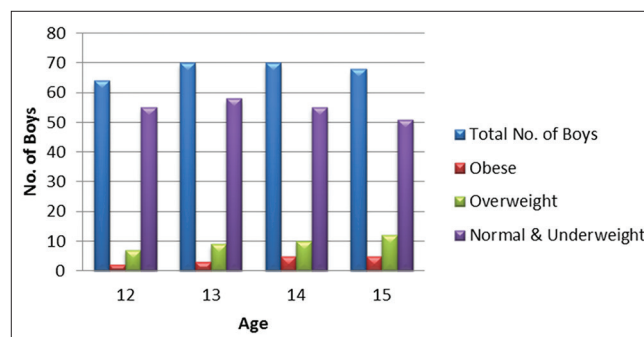
**Figure 1: The prevalence of obesity among girls of rural schools**



**Figure 2: The prevalence of obesity among girls of urban schools**



**Figure 3: The prevalence of obesity among boys of rural school**



**Figure 4: The prevalence of obesity and overweight among urban boys**

in India and abroad. The present study also compares the sex-wise variation seen in children. The prevalence of obesity among boys was found to be higher than that of girls. However, girls were found to be more overweight than boys. Studies by Kapil *et al.* also indicated that the prevalence of obesity was lower in girls (6%) as compared to boys (8%).<sup>4</sup> Kotani *et al.* found that the proportion of obese children in their population had increased from 5% to more than 10% over two decades.<sup>5</sup> All these studies, therefore, indicate that the sex of the child has an influence on the prevalence of overweight and obesity.

The rural and urban population of boys as well as girls were tabulated and significance values calculated. Obesity in girls showed no statistical significance with the urban and the rural population ( $P = 0.964233$ ) Table 5. Boys showed a higher incidence of obesity in the urban setting as compared to the rural population ( $P = 0.000284$ ) (Table 6).

## DISCUSSION

We have found a highly significant increase in the number of overweight and obese children.

The increase in weight and BMI over time has not been accompanied by an increase in height.

In adults, BMI is useful in the assessment of fatness. Concerns have been expressed regarding its use in children because it varies with height and does not take into account the differences in the timing of growth in height and weight among various ethnic groups.<sup>6</sup> Nevertheless, it is easy to measure and has been validated against calculations of body density. For these reasons, it has been recommended by the American Society of Clinical Nutrition and others as a reliable measurement of overweight and obese children.<sup>7</sup>

Obesity increases the likelihood of morbidity and mortality.<sup>8</sup> Calle *et al.* prospectively examined the risk of death related to BMI in over a million adults and concluded that heavier men and women in all age groups had an increased risk of death.<sup>9</sup> Must and Strauss reviewed the risks and consequences of obesity in childhood and adolescence and concluded that an aggressive approach to prevention and treatment was required.<sup>10</sup> Treatment of obesity is most successful if realistic goals are set; a balanced diet is emphasized; a safe rate of weight loss of about 0.5 kg a week is achieved through moderate reduction of energy intake (about 20-25% decrease); increased physical activity

**Table 5: The prevalence of obesity among boys of urban schools**

Group	Age	No	n (%)		
			Obese	Overweight	Normal and underweight
Urban boys	12	64	2 (3.13)	7 (10.94)	55 (85.94)
	13	70	3 (4.29)	9 (12.86)	58 (82.86)
	14	70	5 (7.14)	10 (14.29)	55 (78.57)
	15	68	5 (7.35)	12 (17.65)	51 (75)
Total		272	15 (21.91)	38 (55.74)	80.51

**Table 6: Comparison of obesity among rural and urban boys**

Locale	Obese	Overweight	Normal and underweight	Total
Boys				
Rural	1	12	178	191
Urban	15	38	219	272
Total	16	50	397	463
Expected				
Rural	6.6,00,432	20.6,26,34,989	163.77,32,181	191
Urban	9.3,99,568	29.3,73,65,011	233.22,67,819	272
Total	16	50	397	463
P	0.0,00,284			

is emphasized as much as diet; parental support is strong; and behavior therapy is provided to help both child and parents achieve the diet, exercise, and behavior goals.

Dietary assessment helps to identify both the amount eaten and the child's and family's eating patterns. The prescribed diet should be simple, explicit, and unambiguous so that it is easy to implement and monitor and not subject to confusion or easy rationalization of exceptions. Epstein *et al.* developed the "traffic light diet," which defines all foods by their energy content into red (stop), yellow (proceed with caution), and green (go).<sup>11</sup> Children count the number of servings consumed for each color as well as calories. Three key settings for implementing childhood obesity management support programs have been identified: The family, the school, and primary care. The provision of education on eating and lifestyle behavior to parents has been shown significantly to reduce the prevalence of obesity in children of participating families.<sup>12</sup> By directing preventive efforts at the family of susceptible children, there is the bonus that all members of the family are likely to benefit. Holding classroom lessons on nutrition and physical health was accompanied by improvements in indices of fitness and body fat levels.<sup>13</sup> Nevertheless, maintaining these programs in the school curriculum in the long term has proved difficult owing to competition for school time, the need for teacher supervision, and financial limitations.

The delivery of programs through primary care has received a little formal assessment. Frequent contact with health professionals from an early age has been identified as an important strategy for effective management of obese children through the provision of advice, encouragement, and support for adopting healthy household eating and exercise patterns at an early stage in life.<sup>14</sup> The incidence of childhood obesity is on the increase and obesity most likely will persist into adulthood.<sup>15</sup> It results in considerable morbidity and mortality, especially due to cardiovascular disease. Physical activity, diet regulation in the form of reduction of high fat and high-calorie foods should be encouraged to reduce overweight and obesity.<sup>16-18</sup>

## CONCLUSION

The present findings indicate that prevalence of childhood obesity in Kerala - Ernakulam district is high. However, we found a higher frequency of obesity in boys as compared to the girls which are statistically significant. Obesity is a serious health issue, resulting in both mortality and morbidity. We need to promote early intervention programs which should be aimed at weight reduction. Parents and children must be counseled not to eat junk foods and carbonated drinks. School and college level health education and biannual screening may be of great help in this regard.

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# Calcium-creatinine Ratio and Microalbuminuria in Prediction of Pre-eclampsia

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## Abstract

**Introduction:** Hypertension is one of the most common complications of pregnancy and a leading cause of maternal and perinatal morbidity and mortality. It forms deadly triad along with hemorrhage and infection and contributes greatly to maternal morbidity. An early diagnosis and treatment helps to reduce it to a minimum, and therefore it is important to identify women at risk at the earliest.

**Objectives:** To evaluate the predictive values of urinary calcium-creatinine ratio (CCR) and microalbuminuria for pre-eclampsia.

**Materials and Methods:** Urinary CCR was determined in one step urine sample in 150 asymptomatic pregnant women between 20 and 34 weeks of gestation, who attended the antenatal outpatient department at Indira Gandhi Government Medical College. The results were analyzed by Chi-square test to find the significant association of findings of pre-eclampsia and CCR and microalbuminuria. Area under receiver operator curve was used to find out the predictive values of CCR at  $\leq 0.04$  and microalbuminuria for pre-eclampsia.

**Results:** It was found that CCR had a sensitivity, specificity, positive predictive value, and Negative predictive value of 64%, 96.9%, 80%, and 93.2%, respectively, with  $P < 0.001$  (strongly significant). It was found to be a good test for prediction of pre-eclampsia. Combined microalbuminuria and CCR  $\leq 0.04$  was found to be good tests for prediction of pre-eclampsia ( $P < 0.001$ ).

**Conclusion:** CCR at  $\leq 0.04$  in spot urine sample is a good test for prediction of pre-eclampsia and can be recommended as a screening testing all asymptomatic pregnant women, for pre-eclampsia. Combined CCR and microalbuminuria seem to be effective as a screening tool for pre-eclampsia at present.

**Key words:** Calcium creatinine ratio, Microalbuminuria, Pre-eclampsia

## INTRODUCTION

Hypertension is one of the most common complications of pregnancy and a leading cause of maternal and perinatal morbidity and mortality. It forms deadly triad along with hemorrhage and infection and contributes greatly to maternal morbidity. An early diagnosis and treatment helps to reduce it to a minimum, and therefore it is important to identify women at risk at the earliest.<sup>1</sup>

The etiology of pregnancy-induced hypertension (PIH) is still unclear. There is a diffuse endothelial damage affecting all organs and hypertension is only one of the clinical manifestations of disease. The deleterious effect of PIH on mother and fetus can be prevented by appropriate intervention if PIH is identified early.

Many biochemical and hematological markers have gained recognition in predicting PIH, assessing the severity of disease and in differentiating pre-eclampsia from other hypertensive disorders of pregnancy. We often get women with severe disease at early gestation and many times for mothers health; we have to interrupt the physiological process of pregnancy turning pathological. Hence, the prediction of hypertensive disorder remains only alternative to prevent its disastrous complications.

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Combining the biochemical markers calcium, creatinine, and microalbuminuria, we can predict the risk of disorder and start preventive therapy at early stages to prevent maternal and fetal-neonatal morbidity and mortality.<sup>2,3</sup>

Ideal predictive test should be simple, noninvasive, easy to perform, and reproducible with high sensitivity and specificity. Hence, we choose urinary calcium-creatinine ratio (CCR) and microalbuminuria for prediction of gestational hypertension.

### Aims of the Study

To determine the predictive values of decreasing urinary CCR and microalbuminuria for pre-eclampsia, in spot urine sample, in asymptomatic pregnant women between 20 and 34 weeks of gestation.

## MATERIALS AND METHODS

A total of 150 pregnant women who attended the Indira Gandhi Government Medical College outpatient department for routine antenatal care, over a period of 2-year, between 20 and 34 weeks of gestation were included in the study after obtaining informed consent.

Women with a history of diabetes, chronic hypertension and renal disease were excluded from the study. Women who had proteinuria by dipstick method at the first visit, as well as those with a baseline blood pressure of more than or equal to 140/90 mm of Hg at first visit were excluded from the study.

Blood pressure was measured in semi-recumbent posture with left lateral tilt, in the right arm and proteinuria was excluded by testing a spot sample for albumin by dipstick method.

A spot urine sample was collected for estimation of calcium, creatinine, and microalbumine. Calcium was determined by orthocresolphthalein complex method and urinary creatinine by Jaffe's method.

Microalbuminuria was detected by immunometric assay. All women were followed up till delivery. At each visit, blood pressure was measured and urine was tested for protein by dipstick method. Pre-eclampsia was defined as blood pressure more than or equal to 140/90 mm Hg by using korotkoff 5<sup>th</sup> sound for diastolic BP associated with proteinuria. Based on these criteria women were categorized as those who developed pre-eclampsia and those who remained normotensive.

Calcium to creatinine ratio (CCR) was calculated and those with ratio  $\leq 0.04$  were considered positive. Those with a

ratio of  $>0.04$  were considered as test negative. Women with urinary albumin levels  $>30$  mg/l were considered positive for microalbuminuria and those with  $<30$  mg/l were considered negative for microalbuminuria.

The predictive values of CCR at  $\leq 0.04$  and microalbuminuria were determined by statistical analysis.

### Statistical Analysis

Chi-square test has been used to find a significant association of pre-eclampsia and CCR and microalbuminuria. A  $P < 0.001$  considered strongly significant. Area under receiver operator curve (ROC) has been used to find the predictive values of CCR at  $\leq 0.04$  and microalbuminuria for pre-eclampsia.

## RESULTS

In this prospective clinical study comprising 150 women between 20 and 34 weeks of gestation, the majority (81%) were in the age group of 21-31 years 0.8% were below 21% and 11% were more than 31 years of age. Mean age being  $24.16 \pm 3.14$ .

Incidence of pre-eclampsia in study group was 15% of which 12% had mild, 2.5% severe and 0.5% eclampsia. Mean gestational age at which pre-eclampsia developed was  $37.66 \pm 2.75$ . Among all pre-eclampsia patients, 72% were primigravidas and 28% were multigravida.

Of 150 women studied 25 (16.66%) were test positive, and 125 (83.33%) were test negative (Table 1).

Of 150 women studied 20 (13.33%) were test positive for microalbuminuria ( $>30$  mg/l) and 130 (86.66%) were negative for microalbuminuria ( $<30$  mg/l).

**Table 1: Number of test positive women**

Test parameter	n (%)		Total (%)
	Test positive	Test negative	
CCR	25 (16.66)	125 (83.33)	150 (100)
Microalbuminuria	20 (13.33)	130 (86.66)	150 (100)

CCR: Calcium creatinine ratio

**Table 2: Association of calcium creatinine ratio with pre-eclampsia**

CCR	n (%)		
	Pre-eclampsia	Normotensive	Total
Test positive $\leq 0.04$	16 (64) (True positive)	9 (36) (False positive)	25 (16.66)
Test negative $> 0.04$	4 (3.2) (False negative)	121 (96.8) (True negative)	125 (83.33)
Total	20 (13.33)	130 (86.66)	150 (100)

CCR: Calcium creatinine ratio

**Table 3: Association of microalbuminuria with pre-eclampsia**

Microalbuminuria	n (%)		
	Pre-eclampsia present	Normotensive	Total
Test positive >30 mg/l	11 (7.33) (True positive)	9 (6%) (False positive)	20 (13.33)
Test negative <30 mg/l	5 (3.33) (False negative)	125 (83.33) (True negative)	130 (86.66) (True negative)
Total	16 (10.66)	134 (89.33)	150 (100)

**Table 4: Results of statistical analysis**

Test parameter	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	P
CCR	64	96.9	80	93.2	<0.001**
Microalbuminuria	26.31	92.22	33	87	<0.001

PPV: Positive predictive value, NPV: Negative predictive value, CCR: Calcium-creatinine ratio

Association of CCR and microalbuminuria with pre-eclampsia was determined and is shown in Tables 2 and 3, respectively.

Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated after statistical analysis of the results and are shown in Table 4.

CCR at  $\leq 0.04$  had a sensitivity of 64%, specificity of 96.9%, PPV of 80%, NPV of 93.2% with  $P < 0.001$  which is strongly significant. Microalbuminuria was comparatively less accurate with sensitivity 26.31%, specificity of 92.22%, PPV of 33%, NPV of 87%, with  $P < 0.001$ . Predictive value of CCR and microalbuminuria for pre-eclampsia were calculated using Area under curve of ROC and it was found that CCR at  $\leq 0.04$  was a good test but microalbuminuria was only fair test for prediction of pre-eclampsia.

## DISCUSSION

In our study comprising 150 asymptomatic pregnant women between 20 and 34 weeks of gestation, CCR at  $\leq 0.04$  in spot urine sample had a sensitivity of 64%, specificity of 96.9%, PPV of (PPV) 80%, NPV of 93.2% found and was found to be a good test for prediction of pre-eclampsia.

Rodriguez *et al.*<sup>2</sup> who investigated the predictive value of decreasing CCR in spot urine sample as early as 1988 reported that it might be an effective marker for pre-eclampsia.

Saudan *et al.*<sup>3</sup> had reported the sensitivity of 85% and specificity of 91% and Izumi *et al.*<sup>4</sup> found that it had limited value in prediction of pre-eclampsia.

Kazerooni and Hamje-Nezadi<sup>5</sup> evaluating between 20 and 24 weeks of gestation and Kar *et al.*<sup>6</sup> evaluating the predictive value of CCR at  $\leq 0.04$  between 20 and 34 weeks

of gestation (similar to our study), have reported that it was satisfactory test for prediction of pre-eclampsia and could be effective method for screening asymptomatic women for pre-eclampsia.

Estimation of calcium and creatinine in a spot urine sample is simple test, noninvasive, and is easy to perform and hence assures good patient compliance. It has a good predictive value and hence justifies the cost and is suited to be adopted as screening test for pre-eclampsia. It can, therefore, recommend as a screening test for pre-eclampsia and could be offered to all asymptomatic pregnant women between 20 and 34 weeks of gestation during their routine antenatal visits.

Microalbuminuria, on the other hand, was found to be only fair test in predicting pre-eclampsia with sensitivity, specificity, PPV and NPV of 26.31%, 92.22%, 33% and 87%, respectively.

Salako *et al.*<sup>7</sup> reported that single estimation of microalbuminuria at the time of antenatal booking had a sensitivity of 42% and specificity of 86%.

Chhabra and Gandhi<sup>8</sup> found that estimation of microalbuminuria around 18 weeks of gestation seemed useful, especially in primigravidas. More trials are needed to establish the usefulness of microalbuminuria in prediction of pre-eclampsia before adapting it as screening tool.

Pre-eclampsia is a major cause for concern worldwide, and there is a constant search for finding the means for predicting pre-eclampsia. An availability of good screening test would initiate more research in this direction and will be useful to decrease maternal mortality and morbidity.

## CONCLUSION

A single estimation of CCR at  $\leq 0.04$ , in spot urine sample, in asymptomatic pregnant women between 20

and 34 weeks of gestation have good predictive value and therefore can be recommended as a screening test for all pregnant women. Microalbuminuria, on the other hand is weak test for prediction of pre-eclampsia and cannot be recommended as a screening test at present.

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# Comparative Evaluation of the Efficacy of Preprocedural Mouthrinse and Spray Disinfectant in Reducing Oral Microflora on Corrective Complete Denture Impression: A Crossover Clinical Study

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## Abstract

**Background:** The study was taken up with the aim to identify the micro-organisms transferred on the surface of corrective complete denture impression and to compare the effectiveness of preprocedural mouthrinse in reducing oral microflora in corrective complete denture impression over spray disinfectant.

**Materials and Methods:** The study was conducted on maxillary complete denture impressions made on 30 completely edentulous subjects. A total of 90 impressions were made, and 90 custom trays were fabricated for 30 subjects. These custom trays were divided into three groups: 30 corrective impressions were secured without using mouthrinse (control group), 30 corrective impressions obtained were disinfected with 2% glutaraldehyde (Cidex) for 20 min, and 30 corrective impressions were made after making the subject rinse with hydrogen peroxide mouthwash (hydroxyl) with specified dilution (1:4) for 30 s. The identification of micro-organisms was done using catalase test, oxidase test, and Gram-staining. Student's *t*-test was used for statistical analysis of the study.

**Results:** For the control group, 8 patients showed growth of coagulase –ve *Staphylococcus* and *Streptococcus* viridans; 8 patients showed only *Streptococcus* viridans; in 14 patients only coagulase –ve *Staphylococcus* was found. The data obtained revealed that 18 impressions out of 30 were rendered fully sterile by spray disinfection while the remaining 12 impressions showed a decrease in the colony count of coagulase –ve *Staphylococcus* and *Streptococcus* viridans. Preprocedural mouthrinsing resulted in total elimination of coagulase –ve *Staphylococcus* and *Streptococcus* viridans in 28 impressions while the remaining impressions showed a definite reduction in colony count of these two micro-organisms. 93.33% of the maxillary corrective complete denture impressions secured after preprocedural mouthrinse with hydrogen peroxide showed total elimination of coagulase –ve *Staphylococcus* and *Streptococcus* viridans. Only 60% showed total elimination of micro-organisms for impressions secured after spray disinfection.

**Conclusion:** The study showed that preprocedural mouthrinsing resulted in significant reduction in viable micro-organisms on the surface of the impression.

**Key words:** Maxillary impression, Preprocedural mouthrinsing, Spray disinfectant

## INTRODUCTION

Dentistry is predominantly a field of surgery involving exposure to blood, saliva, and other potentially infectious

materials, and therefore, requires a high standard of infection control and safety.<sup>1</sup>

Analysis of prosthodontic setups shows that many of the instruments and support equipment carry the potential to transmit disease but is not amenable to adequate sterilization or disinfection. Dental practitioners, auxiliaries, and laboratory personnel are subject to significant risk with respect to infectious disease, which can be spread by saliva or blood as droplets and aerosols, or by direct contact.<sup>2</sup>

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Impressions are laden with micro-organisms after removal from the oral cavity, and some of these organisms have the potential for disease transmission.<sup>3,4</sup> Potential pathogens have been isolated from the impressions and organisms have been shown to survive up to 5 h on an impression.<sup>5</sup> The prevalence of these diseases and their potentially harmful effects mandate adherence to infection control procedures in the dental office and laboratory. Dental office personnel may not follow the recommended protocols for disinfecting impressions and other items that come in contact with a patient.<sup>6</sup> Therefore, prosthodontists and the associated personnel are at an added risk of transmission of the infection spreading through contaminated impressions and the casts thus obtained.<sup>7</sup>

Since sterilization of impressions is expensive, time consuming, and potentially damaging to the material, spray disinfection with various chemicals has become a practical alternative.<sup>8</sup> Various studies have focused the intention toward the destruction of micro-organisms with various disinfectants as regard their duration without causing dimensional changes.<sup>1,4,9</sup>

The use of mouthrinse is an effective and feasible way to reduce viable bacteria in the oral cavity.<sup>10</sup> Preprocedural mouth rinsing seems to be one of the most effective methods of controlling the spread of bacteria in the dental office.

According to the Center for Disease Control, "blood and saliva should be thoroughly and carefully cleaned from impression material that has been used in the mouth. Contaminated materials, impression, and intra-oral devices should also be cleaned and disinfected before being handled in the dental laboratory and before they are placed in a patient's mouth."<sup>11</sup> It is imperative that the recommendations for disinfecting dental impressions, presented by the Center for Disease Control be followed.<sup>12</sup> Therefore, the study was taken up with the aim to identify the micro-organisms transferred on the surface of corrective complete denture impression and to compare the effectiveness of preprocedural mouthrinse in reducing oral microflora in corrective complete denture impression over spray disinfectant.

## MATERIALS AND METHODS

The study was conducted in the Department of Prosthodontics, Bhojia Dental College and Hospital, Baddi, Himachal Pradesh, on maxillary complete denture impressions made on 30 suitable completely edentulous subjects of either sex without any recent history of common cold, sore throat, and antibiotic medication.

The study participants were given clear explanation about the objective of the study. Ethical clearance was obtained from the concerned authorities of the institution. Voluntary informed consent was obtained from all the subjects.

Initial impression was made with impression compound. For each subject, three custom trays were fabricated with autopolymerizing acrylic resin on the cast obtained from the impression for each subject. Thus, a total of 90 custom trays were fabricated for 30 subjects. These custom trays were divided into three groups, and corrective impression was secured with zinc-oxide eugenol impression paste.

- Group I (control group): 30 corrective impressions were secured without using mouthrinse
- Group II: 30 corrective impressions obtained were disinfected with 2% glutaraldehyde, (Cidex) for 20 min
- Group III: 30 corrective impressions were made after making the subject rinse with hydrogen peroxide mouthwash (hydroxyl) with specified dilution (1:4) for 30 s.

Saliva sample was collected with sterile swab from each of the zinc-oxide impressions. It was plated on 5% sheep blood agar and then on MacConkey agar. Thereafter with the help of Nichrome loop sterilized on the flame, streaking of both the plates was done. Following this, the plates were kept in candle jar (5% carbon dioxide) and immediately transported to the laboratory.

The candle jar was kept in incubator at 37°C for 48 h. After 48 h, the plates were reviewed for colonies.

Catalase test, oxidase test and Gram-staining were done for all plates.

Catalase test is primarily used to differentiate between genera *Staphylococcus* from *Streptococcus*. Certain bacteria have enzyme catalase which acts on hydrogen peroxide to release nascent oxygen. In catalase test, first of all, a drop of 3% hydrogen peroxide is put on a slide. Then with the help of cover slip, the colonies were taken and touched them with 3% H<sub>2</sub>O<sub>2</sub>. There was bubble formation due to the release of nascent oxygen. *Staphylococcus* is catalase positive and *Streptococcus* is catalase negative.

The principle of oxidase test is to determine the presence of an enzyme cytochrome oxidase which catalyses the oxidation of reduced cytochrome by molecular oxygen. In oxidase test, a slide containing oxidase disc of Hi-Media was taken. Then, the colony was taken from the MacConkey agar plate with a cover slip and touched them with oxidase disc.

Gram staining (or Gram's method) is a method of differentiating bacterial species into two large groups (Gram-positive and Gram-negative). It is based on the chemical and physical properties of their cell walls. Primarily, it detects peptidoglycan, which is present in a thick layer in Gram-positive bacteria.

### Staining Mechanism

Gram-positive bacteria have a thick mesh-like cell wall made of peptidoglycan (50-90% of cell envelope), which are stained purple by crystal violet (CV), whereas Gram-negative bacteria have a thinner layer (10% of cell envelope), which are stained pink by the counter-stain. There are four basic steps of the Gram stain:

- Applying a primary stain (CV) to a heat-fixed smear of a bacterial culture. Heat fixing kills some bacteria but is mostly used to affix the bacteria to the slide so that they do not rinse out during the staining procedure
- The addition of a mordant, which binds to CV and traps it in the cell (Gram's iodine)
- Rapid decolorization with alcohol or acetone, and
- Counterstaining with safranin. Carbol fuchsin is sometimes substituted for safranin since it will more intensely stain anaerobic bacteria but it is much less commonly employed as a counterstain. CV dissociates in aqueous solutions into CV<sup>+</sup> and chloride (Cl<sup>-</sup>) ions. These ions penetrate through the cell wall and cell membrane of both Gram-positive and Gram-negative cells. The CV<sup>+</sup> ion interacts with negatively charged components of bacterial cells and stains the cells purple.

Iodine (I<sup>-</sup>) interacts with CV<sup>+</sup> and forms large complexes of CV and iodine (CV-I) within the inner and outer layers of the cell. Iodine is often referred to as a mordant but is a trapping agent that prevents the removal of the CV-I complex, and therefore, colors the cell.

When a decolorizer such as alcohol or acetone is added, it interacts with the lipids of the cell membrane. A Gram-negative cell will lose its outer lipopolysaccharide membrane, and the inner peptidoglycan layer is left exposed. The CV-I complexes are washed from the Gram-negative cell along with the outer membrane. In contrast, a Gram-positive cell becomes dehydrated from an ethanol treatment. The large CV-I complexes become trapped within the Gram-positive cell due to the multilayered nature of its peptidoglycan. The decolorization step is critical and must be timed correctly; the CV stain gets removed from both Gram-positive and negative cells if the decolorizing agent is left on too long (a matter of seconds).

After decolorization, the Gram-positive cell remains purple and the Gram-negative cell loses its purple color.

Counterstain, which is usually positively charged safranin or basic fuchsin, is applied last to give decolorized Gram-negative bacteria a pink or red color.

### Identification of Micro-organisms

Catalase positive *Staphylococcus* is identified by slide coagulase test. In slide coagulase test, a drop of normal saline 0.85% was put. Then with a nichrome loop, a colony from the McConkey/blood agar was taken and mixed with normal saline. After it, a drop of plasma was added and looked for agglutination. If agglutination was present, it indicated coagulase positive *Staphylococcus aureus* and in the absence of agglutination, the micro-organism identified was coagulase-negative *Staphylococcus* which is a normal microflora in humans.

Catalase negative *Streptococcus viridans* (normal microflora) are identified by its partial discoloration on blood agar and greenish tinge around colonies. If there is complete hemolysis of catalase negative *Streptococcus*, it indicates *Streptococcus pyogenes* which is a pathogen. If no hemolysis occurs, it indicates Group D *Streptococcus*.

In oxidase test, change to violet/purple color indicated oxidase positive micro-organisms.

Gram-positive bacteria are arranged in chains, few in packs and few in bunches.

### Statistical Analysis

Student's *t*-test was used for statistical analysis of the study. The  $P < 0.05$  was accepted as indicating statistical significance and  $P \leq 0.001$  was noted as highly significant. Student's *t*-test was used to find a significant difference between two means. The results were averaged (mean  $\pm$  standard deviation) for each parameter.

## RESULTS

Subject categorization was done (Table 1) and a total of 90 impressions were made for 30 patients.

The micro-organisms identified in 30 patients are presented in Figures 1 and 2, Table 2. For the control group, 8 patients showed growth of coagulase -ve *Staphylococcus* and *Streptococcus viridans*; in 8 patients only *Streptococcus viridans* was found. In 14 patients, only coagulase -ve *Staphylococcus* was found. The data obtained revealed that 18 impressions out of 30 were rendered fully sterile by spray disinfection while the remaining 12 impressions showed a decrease in the colony count of coagulase -ve *Staphylococcus* and *Streptococcus viridans*. The most striking feature was the total elimination of coagulase -ve *Staphylococcus* and *Streptococcus viridans* in 28 impressions after preprocedural mouthrinsing while the

**Table 1: Distribution of groups**

Groups	Procedure	Total
I	No preprocedural mouthrinsing or spray disinfection of corrective impression	30
II	Spray disinfection of corrective impression	30
III	Corrective impression after preprocedural mouthrinse	30

**Table 2: Colony count in each subject**

Colony count for control group	Colony count after disinfection	Colony count after mouthwash
<i>Streptococcus viridans</i> >10 <sup>5</sup> mg/ml	3.7×10 <sup>4</sup> organisms/ml	Sterile
Coagulase-ve <i>Staphylococcus</i> >10 <sup>5</sup> mg/ml	Sterile	Sterile
Coagulase-ve <i>Staphylococcus</i> >10 <sup>5</sup> mg/ml	Sterile	Sterile
Coagulase-ve <i>Staphylococcus</i> >10 <sup>5</sup> mg/ml	Sterile	Sterile
Coagulase-ve <i>Staphylococcus</i> >10 <sup>5</sup> mg/ml	Sterile	Sterile
<i>Streptococcus viridans</i> >10 <sup>5</sup> mg/ml and coagulase-ve <i>Staphylococcus</i> >10 <sup>5</sup> mg/ml	4.8×10 <sup>4</sup> org/ml	Sterile
<i>Streptococcus viridans</i> >10 <sup>5</sup> mg/ml	Sterile	Sterile
Coagulase-ve <i>Staphylococcus</i> >10 <sup>5</sup> mg/ml	Sterile	Sterile
<i>Streptococcus viridans</i> >10 <sup>5</sup> mg/ml and coagulase-ve <i>Staphylococcus</i> >10 <sup>5</sup> mg/ml	7.2×10 <sup>4</sup> org/ml	Sterile
<i>Streptococcus viridans</i> >10 <sup>5</sup> mg/ml	5.5×10 <sup>4</sup> org/ml	Sterile
<i>Streptococcus viridans</i> >10 <sup>5</sup> mg/ml	8.8×10 <sup>4</sup> org/ml	Sterile
<i>Streptococcus viridans</i> >10 <sup>5</sup> mg/ml and coagulase-ve <i>Staphylococcus</i> >10 <sup>5</sup> mg/ml	5.4×10 <sup>4</sup> org/ml	Sterile
Coagulase-ve <i>Staphylococcus</i> >10 <sup>5</sup> mg/ml	2.4×10 <sup>4</sup> org/ml	Sterile
<i>Streptococcus viridans</i> >10 <sup>5</sup> mg/ml and coagulase-ve <i>Staphylococcus</i> >10 <sup>5</sup> mg/ml	6.4×10 <sup>4</sup> org/ml	Sterile
<i>Streptococcus viridans</i> >10 <sup>5</sup> mg/ml and coagulase-ve <i>Staphylococcus</i> >10 <sup>5</sup> mg/ml	4.5×10 <sup>4</sup> org/ml	Sterile
Coagulase-ve <i>Staphylococcus</i> >10 <sup>5</sup> mg/ml	7.8×10 <sup>4</sup> org/ml	Sterile
Coagulase-ve <i>Staphylococcus</i> >10 <sup>5</sup> mg/ml	Sterile	Sterile
Coagulase-ve <i>Staphylococcus</i> >10 <sup>5</sup> mg/ml	Sterile	Sterile
Coagulase-ve <i>Staphylococcus</i> >10 <sup>5</sup> mg/ml	Sterile	Sterile
Coagulase-ve <i>Staphylococcus</i> >10 <sup>5</sup> mg/ml	Sterile	Sterile
<i>Streptococcus viridans</i> >10 <sup>5</sup> mg/ml and coagulase-ve <i>Staphylococcus</i> >10 <sup>5</sup> mg/ml	Sterile	Sterile
Coagulase-ve <i>Staphylococcus</i> >10 <sup>5</sup> mg/ml	4×10 <sup>4</sup> org/ml	3.2×10 <sup>4</sup> org/ml
<i>Streptococcus viridans</i> >10 <sup>5</sup> mg/ml	Sterile	Sterile
<i>Streptococcus viridans</i> >10 <sup>5</sup> mg/ml	Sterile	Sterile
<i>Streptococcus viridans</i> >10 <sup>5</sup> mg/ml and coagulase-ve <i>Staphylococcus</i> >10 <sup>5</sup> mg/ml	Sterile	Sterile
<i>Streptococcus viridans</i> >10 <sup>5</sup> mg/ml and coagulase-ve <i>Staphylococcus</i> >10 <sup>5</sup> mg/ml	7×10 <sup>4</sup> org/ml	5×10 <sup>4</sup> org/ml
<i>Streptococcus viridans</i> >10 <sup>5</sup> mg/ml	Sterile	Sterile
Coagulase-ve <i>Staphylococcus</i> >10 <sup>5</sup> mg/ml	Sterile	Sterile
Coagulase-ve <i>Staphylococcus</i> >10 <sup>5</sup> mg/ml	Sterile	Sterile
<i>Streptococcus viridans</i> >10 <sup>5</sup> mg/ml	Sterile	Sterile

remaining 2 impressions showed a definite reduction in colony count of these two micro-organisms.

About 93.33% of the maxillary corrective complete denture impressions secured after preprocedural mouthrinse with hydrogen peroxide showed total elimination of coagulase -ve *Staphylococcus* and *Streptococcus viridans*. For impressions secured after spray disinfection, 60% showed total elimination of micro-organisms.

Pairing of samples was done (Tables 3 and 4). According to statistical analysis a highly significant ( $P < 0.001$ ) reduction in colony count of bacteria was observed in pair 3, a significant reduction in pair 2 and a reduction in pair 1. Thus, greatest reduction in the colony count was found in the pair comparing preprocedural mouthwash and disinfection.

## DISCUSSION

The aim of the study was to assess the efficiency of a 30-s preprocedural mouthrinse with hydrogen peroxide mouthwash (1:4) over 2% glutaraldehyde spray disinfection for 20 min in reducing viable coagulase -ve *Staphylococcus* and *Streptococcus viridans* in maxillary corrective complete denture impression secured with zinc-oxide eugenol impression paste.

The disinfection of impressions is a standard recommendation for infection control procedures in prosthodontics. Concerns have been expressed about the effects of disinfection on the impression materials. Research has shown that disinfection process may cause degradation or distortion of the impressions. Nevertheless, the American Dental Association (ADA)

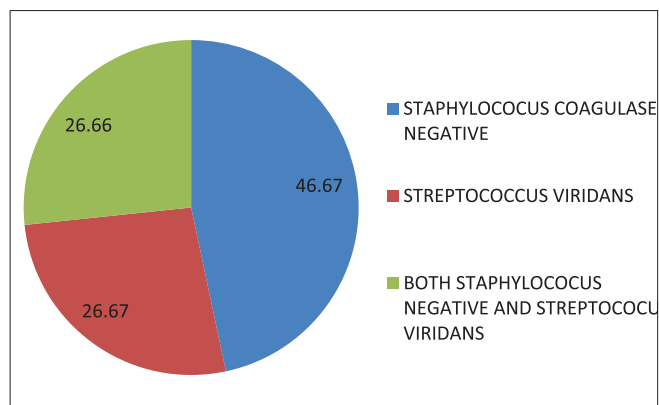


Figure 1: Micro-organisms identified

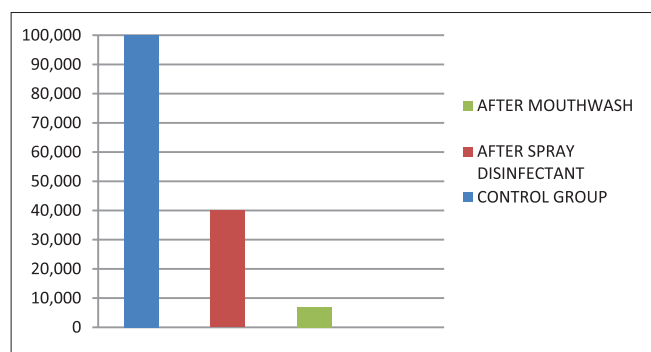


Figure 2: Colony forming units

currently recommends immersion or spray disinfection with an ADA-accepted disinfectant for the manufacturer's recommended contact time.<sup>13</sup> Kern *et al.* demonstrated the effectiveness of glutaraldehyde in reducing micro-organisms on impression materials.<sup>14</sup>

Look *et al.* reported that although 2% glutaraldehyde achieved total viral inactivation in <1 min, short disinfectant sprays, in general, are not an appropriate disinfection method.<sup>2</sup>

de Albuquerque *et al.* in their study found that single preprocedural chlorhexidine mouthrinse is effective in reducing salivary micro-organisms.

The authors demonstrated that low-concentration, 30-s chlorhexidine mouthrinses could be an easy and inexpensive method to help reduce postoperative infections by lowering oral counts of *S. aureus* and mutans group streptococci.<sup>15</sup>

Wennström and Lindhe J studied the effect of hydrogen peroxide release during mouth rinsings on the composition of the microbiota of developing plaque in humans and the amount and pathogenicity of the plaque formed. The authors suggested that hydrogen peroxide released by mouthwashes during rinsing may prevent or

Table 3: Pairing of samples (t-test)

Paired samples statistics	Mean	n	Standard deviation	Standard error mean
Pair 1				
Colony count for control group	100,000.0000	30	0.00000	0.00000
Colony count after disinfection	22,500.0000	30	30,306.19602	5533.12906
Pair 2				
Colony count for control group	100,000.0000	30	0.00000	0.00000
Colony count after mouthwash	2733.3333	30	10,667.16953	1947.54979
Pair 3				
Colony count after disinfection	22,500.0000	30	30,306.19602	5533.12906
Colony count after mouthwash	2733.3333	30	10,667.16953	1947.54979

Table 4: Pairing of samples (t-test)

Paired samples test	Paired differences						t	df	Significant (2-tailed)
	Mean	Standard deviation	Standard error mean	95% confidence interval of the difference					
				Lower	Upper				
Pair 1									
Colony count for control group-Colony count after disinfection	77500.00000	30306.19602	5533.12906	66183.48042	88816.51958	14.007	29	0.042*	
Pair 2									
Colony count for control group-Colony count after mouthwash	97266.66667	10667.16953	1947.54979	93283.48010	101249.85323	49.943	29	<0.006*	
Pair 3									
Colony count after disinfection-Colony count after mouthwash	19766.66667	28806.94760	5259.40500	9009.97565	30523.35768	3.758	29	<0.001**	

\*P<0.05, \*\*P<0.001

retard the colonization and multiplication of anaerobic bacteria.<sup>16</sup>

Therefore, the use of mouthrinses is an effective and feasible way to reduce viable bacteria in the oral cavity. Preprocedural mouth rinsing seems to be one of the most effective methods of controlling the spread of bacteria in the dental office, and some studies have addressed this topic.<sup>10</sup>

Similarly, in prosthodontics mouthrinsing before impression making with a recommended mouthwash may be employed as an effective infection-control procedure. This procedure may put an end to various contradictions regarding the dimensional stability and accuracy of impression material subject to spray or immersion disinfection. It may be potent in preventing cross-contamination, and therefore, reduces the dangers involved in the spread of certain infectious diseases to the prosthodontists, ancillary, and the laboratory personnel.

Chacra *et al.* in their study found that by decreasing colonization of bacteria, hydrogen peroxide promotes local hygiene. Hydrogen peroxide improves coagulation and decreases the incidence of bleeding without side effects.<sup>17,18</sup> Furthermore, hydrogen peroxide mouth rinse contains no alcohol, and thus, does not dry out the oral cavity.

The hydrogen peroxide mouthwash is generally used to fight and prevent various oral harmful bacteria and infections. It is thought to decrease colonization of bacteria and infection, thereby decreasing the severity and duration of pain. It has further shown enhanced wound healing following gingival surgery.<sup>17</sup>

The results of this study proved the impressive efficacy of hydrogen peroxide mouthwash. In 93.33 % of the maxillary corrective complete denture impressions secured after preprocedural mouthrinse with hydrogen peroxide, there was total elimination of coagulase –ve *Staphylococcus* and *Streptococcus viridans*. While for impressions secured after spray disinfection the success rate was 60%. Thus, indicating preprocedural mouthrinsing better than spray disinfection. The factor that needs to be emphasized here is that superior efficacy of preprocedural mouthrinse is free from any objections regarding the integrity of the impressions obtained in this manner. It is important to mention that the preprocedural mouthrinsing infection-control method, i.e., before impression making in completely edentulous mouth has not been addressed often if not ever in the literature available.

- The limitation of the study was that only healthy patients were included in the sample size. Therefore, only the normal oral micro-organisms were evaluated

- Within the limitations of the study, preprocedural mouthrinsing can be used as an aid to prevent cross-contamination and infection-control procedure in prosthodontics. Uncompromising dimensional accuracy and stability of the impressions obtained in this manner is the major benefit of this procedure. In addition, it has a chemotherapeutic role without any known side effect on the oral hygiene of an edentulous mouth and is quite economical.

## CONCLUSION

The study showed that preprocedural mouthrinsing was found to an effective measure for lowering the viable micro-organisms on the surface of the impression.

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# Outcome of High-energy Tibial Plateau Schatzker Type VI Fractures with Compromised Soft Tissue Treated by Ilizarov Fixator

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## Abstract

**Background:** High-energy fractures of tibial plateau are associated with severe articular depression, separation of both condyles, diaphyseal comminution and dissociation and loss of integrity of the soft-tissue envelope. Complications of plating are well known since last 50 years in these difficult fractures. An alternative method was proposed by Ilizarov (Catagni, 1991; Ilizarov, 1992), and we have adopted his techniques for the treatment of these complex injuries.

**Aim of Study:** This prospective study used this method, i.e., Ilizarov fixator for the management of high-energy fractures of the tibial plateau.

**Material and Methods:** A total of 13 patients (mean age of 44 years) with high-energy fractures of the tibial plateau (Schatzker VI) by the Ilizarov fixator and transfixion wires. 7 fractures were open, and 6 patients had complex injuries. All were treated by ligamentotaxis and percutaneous fixation. All were followed for a mean of 24 months.

**Results:** All the fractures united with an average time to healing of 15 weeks. Eight patients achieved full extension and 5 patients more than 110° of flexion. All knees were stable with one patient uniting in mild varus deformity. 12 patients walked normally and one patient with only a slight limp. All but one knee had an articular step-off of <4 mm and all had normal axial alignment except one. Using the knee society clinical rating system, six knees were rated as excellent, four as good, one as fair, and one as poor. There were no cases of post-operative skin infection, osteomyelitis, or septic arthritis. There was a direct correlation between the presence of associated injuries and the final outcome.

**Conclusion:** The technique is well suited to the management of complex fractures of the tibial plateau when extensive dissection and internal fixation are contraindicated due to the comminution at the fracture site and compromise of the soft tissue.

**Key words:** Ilizarov, Ligamentotaxis, Metaphyseal fractures, Schatzker

## INTRODUCTION

Complex tibial plateau fractures are one of the most challenging problems in fracture surgery.<sup>1-3</sup> In 1979, Schatzker *et al.* described six types of tibial plateau

fractures based on anteroposterior (AP) radiographs.<sup>4</sup> Schatzker Type VI tibial plateau fractures are caused by severe high-energy trauma. A transverse or oblique fracture of proximal tibia is present in addition to a fracture of one or both condyles of the tibia and articular surfaces. The high energy causes severe bony comminution and soft tissue injury. These high energy injuries cause significant articular depression, condylar displacement, metadiaphyseal fracture extension with open wounds or extensive closed degloving injuries of the proximal tibia.<sup>5</sup> Complications include severe soft tissue coverage problems, lower limb compartment syndrome, peroneal nerve injury, vascular injury, and eventual knee arthrosis.<sup>6</sup>

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These associated complications directly impact surgical decision-making and prognosis.

The principles of the treatment are anatomical reconstruction of the articular surface, restoration of the anatomical axis, fixation spanning the metaphyseal comminution, and further minimization of secondary insult to an already traumatized soft tissue envelope.<sup>7</sup> These objectives can be achieved with internal fixation or external fixation with or without limited open procedures and bone grafting or a combination of these methods. With extensive contusion or soft-tissue injury, a joint-bridging external fixator is recommended to provide a sufficient stability for the recovery of the soft tissues. The concept of “spanning” the knee joint was introduced in the 1990s.<sup>5</sup> This concept evolved as proponents of indirect fracture reduction and biological fixation reported increased rates success.<sup>8</sup> With this method, the fractures are indirectly reduced with traction, and then maintained with either internal or external fixation before a knee-spanning external fixator is finally applied. With the knee-spanning external fixator, reduction of the intra-articular fragments is maintained.

Many problems encountered in the management of such fractures has panacea in Ilizarov technique. It provides a method for closed reduction and fixation that does not necessitate excessive soft-tissue stripping.<sup>1-3,9-11</sup> Combining this Ilizarov external fixation with minimal internal fixation provides better radiological and functional results.<sup>11,12</sup> The aim of this study was to assess the clinical outcomes of Type VI tibial plateau fractures with severe soft tissue injuries treated with Ilizarov spanning fixator across the knee joint.

## MATERIALS AND METHODS

A total of 15 patients were included in this prospective study conducted between 2011 and 2014. The average was 36 years (range 18-65 years). There were 13 male and 2 female patients. The mode of injury was road traffic accident in all cases. There were open fractures in 9 cases and closed fractures with large blisters in 6 cases. The open fractures were Gustilo-Anderson Type I in 2 cases, Type II in 5 cases, and Type III in 2 cases.<sup>10</sup> Six closed fractures had extensive closed soft tissue injuries (mostly Type I and II Tschern and Gotzen).<sup>13</sup> All patients with the presence of high-energy tibial plateau fractures (Schatzker VI) either closed or open in skeletally mature patients were included. AP view X-ray was used to determine medial and lateral plateau involvement with a degree of articular comminution and lateral view X-rays were used to determine the extent of posterior displacement of condyles and joint depression. Soft tissue condition had a crucial importance on our

planning for the time of the operation. All patients were reviewed at a minimum of 12 months.

The patients with open fractures ( $n = 9$ ) patients were operated within 6 days after primary wound irrigation, debridement, and intravenous antibiotics; while 6 closed fractures were treated with an average of 4 days delay (range 3-6 days) to allow soft tissue edema to subside. In cases of extremely complex and unstable fractures ( $n = 13$ ), the frame was extended onto the distal femur which kept the knee joint in distraction.

### Operation Technique

The operation was done under spinal anesthesia in radiolucent operating table. The fragments were aligned by simple manual traction by an assistant or by fracture table. The fracture reduction was visualized on both planes by the image intensifier. Fragments were held with patella holding forceps. Depressed articular fragments often necessitate elevation (2 cases). The failure to reduce the articular fragments often necessitates an open reduction. A small window was made over tibial cortex through a small incision on the anterior-medial aspect of the tibial metaphysis. A bone elevator was introduced through the hole and fragments were elevated under image intensifier. Meniscal or ligament injuries were not addressed at this stage. After reduction of the condyles, counteropposed olive wires through the fragments were used to achieve interfragmentary compression. Three wires with a divergence of at least 60° were usually required for stabilization of the condylar and metaphyseal fragments. The wires were placed at least 15 mm away from the joint surface to prevent synovial contact and to avoid septic arthritis in the case of pin tract infection. The first 1.8 mm olive wire was inserted using image intensifier in a lateral to medial direction just anterior to the head of the fibula at the tibial plateau subchondral region to provide interfragmentary compression. All wires were passed through safe zones. The first ring was fixed to the first wire with two fixation bolts and tensioned to create compression in between the articular fragments. Another olive wire was applied from medial to lateral on the distal side of the ring, and then a drop wire is inserted. This ring is then connected to one ring distally with four interconnecting rods. Care was taken to restore the mechanical axis in relationship to the condyles. The frame was extended as distractor onto the distal femur. The frame was fixed by two half pins between quadriceps and hamstring. The tibial and femoral rings were connected with connecting rods. The pin sites were dressed with povidone-iodine solution soaked gauzes.

### Post-operative Rehabilitation

For open fractures, either daily dressing or delayed primary closure or skin grafting was done depending on the size

of the wound. Post-operative care consisted of daily pin tract dressing. Check radiographs were done on the next day and adjustments of the fixator were done by the 3<sup>rd</sup> day. Parenteral antibiotics were given up to the 3<sup>rd</sup> day for closed fractures and up to the eradication of infection or wound healing for open and infected fractures. Active and passive dorsiflexion exercises of the ankle were started on the second post-operative day. To prevent an equinus deformity of the ankle, the foot was kept in a neutral position by splinting. Isometric quadriceps exercises and hip raising exercises were permitted. All patients were allowed partial weight bearing as pain tolerated by the end of 1 week. Patients with open fractures were checked weekly in the outpatient department until wound healing. Thereafter, they were checked every 4 weeks (as patients with closed fractures) with check radiographs. The femoral frame was removed on an average 4.4 weeks after the operation and knee range of motion (ROM) exercises were allowed. All patients were encouraged to fully weight-bear. After radiographic healing, frame dynamization was performed to decrease pin bone stresses and to transmit weight-bearing forces to the bone. Incomplete fracture healing was assumed when pain or subtle radiographic changes were present after frame dynamization. The frame was retightened to allow further consolidation. The external fixator was removed once radiographic evidence of union was established, and the fracture was clinically united. Clinically, healing was defined as the ability to bear full weight with a varus and valgus stress to the injured tibia without causing pain. All the fixators were removed as an outpatient procedure without anesthesia. Walking cast was applied for 3-4 weeks. Physiotherapy was continued after removal of the cast to improve the range of knee motion. Radiographs were taken without cast and were allowed full weight bearing with follow-up at 6 weeks, 3, 6 and 12 months.

### Assessment

All patients had record of the clinical and subjective assessment, the level of function and radiological assessment according to the criteria established by Honkonen and Järvinen (1992).<sup>14</sup> All patients were asked to record their symptoms electrical submersible pumps frequency and importance. The symptoms were pain during activities, swelling, stiffness, weakness, limping, giving way, and crepitus. The severity was assessed by multiplying the frequency of symptoms by the grade of importance to the patient. All patients were clinically assessed with extension lag (in degrees), flexion range (in degrees), and thigh atrophy (in cm). These parameters are graded from excellent to poor. The final score was the lowest grade found in any of the four tests. Functional assessment was done by assessing the walk, stair climbing, squatting,

jumping and duck-walking. The final score was the lowest found on these five tests and graded as excellent to poor. Radiological grading was done by assessing the plateau tilt, varus/valgus tilt, articular step-off, condylar widening, and degeneration (relative narrowing of the joint). The radiographs were assessed in both AP and lateral planes. Tilting of the plateau was measured in the frontal plane by drawing a line between the deepest points of the weight-bearing area of the two condyles. The angle between that line and the long axis of the tibia was recorded. Local step-off was measured whenever there was an intact part of the articular surface. The normal alignment of the plateau was measured on the radiograph of the uninjured knee. Condylar widening was estimated in comparison with the width of the ipsilateral femoral condyles. Posttraumatic arthritis was recorded as narrowing of the joint space compared with the uninjured knee.

## RESULTS

The mean interval between the injury and application of the Ilizarov ring external fixator was 5.6 days (range 3.5-10 days) in our hospital. The external fixator was tolerated for the entire treatment period in all cases. Average partial weight bearing walking was 5.5 days (range 4-7 days), and average full weight bearing was 17.4 weeks (15-25 weeks). The mean hospital stay was 5.4 weeks (range 2-18 weeks). All fractures healed with an average time of treatment with the frame for 14.6 weeks (range 10.5-45 weeks). All but two fractures were united within 4 months. 11 patients required additional casting and four patients did not require any other form of supports. In one patient, fracture took longer than 6 months to heal. Two patients had pin track infection. All pin track infections healed by regular dressing without requiring wire removal. One patient had united in varus (10°) but was asymptomatic. One patient required muscle flap procedure for soft tissue coverage, and two patients required split-thickness skin grafting.

A total of 14 patients regained functional use of the knee joint, without pain or instability and improved quality of daily living. Mean flexion of 110° (range 70-130°) was achieved in 15 patients at a mean follow-up of 19.4 months. In fractures treated with knee distractor ( $n = 13$ ), the average knee flexion achieved was 108° (range 70-130°). 2/15 patients were able to flex the knee 130° and 6/15 patients up to 120°. Three patients had 5° lack of extension (range 0-8°). Thigh atrophy of more than 1 cm was noted in only one patient.

Normal walking was observed in nine patients and four had a mild limp. None of the patients used any walking aid. Squatting was normal in 10 patients. Limitation of squatting

was observed in three patients. 8/15 patients could climb stairs normally. Overall, there were seven excellent, seven good and one fair result.

On AP radiographs, the varus tilt of  $10^\circ$  was noted in one patient. On lateral radiographs, the plateau tilt of  $<6^\circ$  was noted in two patients. Only one patient had a step of  $<4$  mm on the articular surface. On comparing with the uninjured knee, the tibial varus tilt was observed in two patients. Condylar widening was noted in 7 patients and none were more than 6 mm. No patients had post-traumatic degeneration. Radiologically, 6 were excellent, 4 were good, and 4 were fair (Tables 1-3) (Figures 1-4).

## DISCUSSION

Decision-making in the management of tibial plateau Schatzker Type VI fractures with extensive soft tissue injuries relates to the long-term outcome.<sup>15</sup> Surgery is indicated in such fractures with metaphysis-diaphyseal dissociation.<sup>16</sup> In this series, 60% patients had open fractures and 40% had significant closed injuries to the soft tissue. Joint spanning circular fixation (Ilizarov frame) provides adequate healing of soft tissue injuries especially ligament injuries. In the present series, despite the severe articular comminution, spanning of fixator across the

joint allowed adequate rest to the tissues and a satisfactory functional outcome was achieved. It has been reported that the healing of the articular surface is adequate when the articular congruity is maintained. Intra-operative



Figure 1: Pre-operative X-ray



Figure 2: Fracture fixed with Ilizarov ring

**Table 1: Number of patients with grades of fractures with time to union**

Grade	Number of patients	Time to union (weeks)
I <sup>a</sup>	2	12
II <sup>a</sup>	5	14.6
III <sup>a</sup>	2	20
I <sup>b</sup>	2	13
II <sup>b</sup>	4	14

<sup>a</sup>Open fractures (Gustillo/Anderson), <sup>b</sup>Closed fractures (Tscherne/Goetzten)

**Table 2: Details and outcome in 15 patients with Schatzker VI fractures**

Age	Sex	Side	Soft tissue status	Fixator (weeks)		Full weight bearing (week)	Follow-up (months)	Time to union (week)	Range of motion (°)	Results	Complication
				Femoral	Tibial						
36	Male	Left	Blister	No	12	15	24	14	120	Excellent	No
39	Male	Right	Open	4	13	16	18	15	120	Excellent	No
53	Male	Left	Open	6	16	25	30	25	70	Fair	Stiffness
63	Male	Left	Blister	4	13	17	18	15	100	Good	Pin tract infection
48	Female	Right	Open	4	14	17	18	15	120	Excellent	Pin tract infection
44	Male	Left	Blister	4	13	16	24	13	130	Excellent	No
37	Male	Right	Open	4	14	17	16	14	100	Good	Varus deformity
27	Male	Left	Open	6	18	20	16	16	100	Good	No
50	Male	Left	Blister	6	12	15	15	13	120	Excellent	No
25	Male	Right	Open	4	16	17	20	14	120	Excellent	No
60	Male	Left	Blister	4	13	17	18	13	100	Good	No
45	Female	Right	Open	4	14	17	18	15	120	Good	No
42	Male	Left	Blister	4	13	16	24	13	130	Excellent	No
33	Male	Right	Open	4	14	17	16	12	100	Good	No
31	Male	Left	Open	No	18	19	16	12	100	Good	No



**Figure 3: Post-operative radiological outcome**



**Figure 4: Post-operative functional range of motion**

**Table 3: Outcome analysis of individual ailments**

Subjective outcome	Clinical outcome	Functional outcome	Radiological outcome
Good	Excellent	Excellent	Excellent
Good	Excellent	Excellent	Excellent
Poor	Fair	Fair	Poor
Fair	Good	Good	Fair
Good	Excellent	Good	Excellent
Excellent	Excellent	Excellent	Excellent
Fair	Good	Good	Fair
Fair	Good	Good	Fair
Good	Excellent	Excellent	Excellent
Good	Excellent	Excellent	Excellent
Fair	Fair	Good	Good
Good	Good	Good	Good
Excellent	Excellent	Excellent	Good
Fair	Good	Fair	Fair
Fair	Good	Good	Good

imaging helps in providing congruous reduction although it is difficult to achieve an anatomical reduction by closed methods. Instability of the knee after these fractures is a major cause of a poor result.<sup>15,17-19</sup> Whether it is due

to ligamentous laxity or bone deformity is debatable.<sup>18,20</sup> There is no general agreement as to whether the repair of associated ligament injuries at the time of the fixation of the fracture is necessary, but many believe that operative repair should be undertaken.<sup>19,20</sup> In this series, the ligament injuries were not primarily assessed. Ilizarov circular fixation allowed both early movement and early weight-bearing, and none of the patients had signs of instability.

Open reduction and internal fixation are not indicated in the presence of fracture blisters or extensive subcutaneous hemorrhage and bruising. Literature review suggests increased rates of infection in 23-80% patients with complex proximal tibial fracture.<sup>21-24</sup> Morandi *et al.* showed decreased the rate of complications with external fixation in such fractures.<sup>25</sup> The percutaneous wires could be used to avoid additional devitalization of the bone since the periosteal and endosteal blood supply do not undergo a secondary insult. Olive wires act as lag screws and compress the fragments against condyle. Small tension wire helps to hold the small fragments.<sup>26</sup> Mechanical axis of lower limb can be maintained and monitored by adjustment of the frame. Two patients required open reduction with an elevation of the tibial plateau. Early ROM in such fractures has been well established,<sup>16</sup> but early loading of such fractures has generally been avoided because the reduction may be lost, resulting in depression of the joint surface or a progressive deformity. However, early weight bearing could stimulate bone healing and muscular strength could be regained early for a better functional outcome.<sup>25</sup> The Ilizarov tibiofemoral frame allows initial weight bearing. In this series, it has been observed that minimum of 6 weeks was required for soft callous formation. The early sign of healing due to early weight bearing confirms the already established theory.<sup>27</sup>

Our study emphasises, the low morbidity associated with the Ilizarov method. No patient developed osteomyelitis or septic arthritis. This absence of infection and septic nonunion compares favorably with other published studies on these complex injuries.<sup>28,29</sup> The functional outcome of tibial plateau fractures managed with Ilizarov fixator was reported as excellent to good in 76-89%.<sup>30-32</sup> In this series, excellent to good function was achieved in 96.7% patients. Kumar and Whittle in a study of treatment of complex fractures of the tibial plateau with circular wire external fixation had reported an average of 173 days, i.e., 24.71 weeks (range 50-415 days) for fracture union, i.e., 7.14-59.28 weeks.<sup>33</sup> Behrens and Searls in their study of external fixation of the tibia showed average union time of 186 days, i.e., 26.57 weeks.<sup>34</sup>

In our study, knee flexion in knee distractor group was 108.4° compared with average 83° in El Barbary *et al.*<sup>29</sup>

## CONCLUSION

The technique is well suited to the management of complex fractures of the tibial plateau when extensive dissection and internal fixation are contraindicated due to the comminution at the fracture site and compromise of the soft tissue.

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# Determination of the Effectiveness of Enhanced Recovery after Surgery Protocols in Patients Undergoing Emergency Laparotomies

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## Abstract

**Introduction:** Enhanced Recovery after Surgery (ERAS) protocol is a combination of evidence-based perioperative strategies which work synergistically to expedite recovery after surgery.

**Aim:** To compare the post-operative recovery rate using ERAS and Institutional standard protocol.

**Materials and Methods:** A prospective case-control study was conducted to compare the recovery rate of ERAS protocol with institutional standard protocol.

**Results:** A total of 25 patients in each group, Group A undergo institutional standard protocol and Group B in ERAS protocol method. When compared with Group A, the patients in Group B shown normal bowel movement in 3.44 days, duration of hospital stay was 7.88 days, pain score was 2.08 which is better than Group A.

**Conclusion:** ERAS protocol has shown earlier post-operative recovery rate than institutional standard protocol.

**Key words:** Enhanced Recovery after Surgery, Enhanced recovery, Postoperative care, Fast track protocol

## INTRODUCTION

Recent efforts to improve the patient outcomes and in reducing the hospital of the patients focus mainly on enhancing the post-operative recovery with a multimodal approach. The concept of fast-track surgery, which is also called enhanced recovery after surgery (ERAS) or multimodal surgery involves the usage of various strategies to enable better conditions for surgery and recovery to achieve faster discharge from hospital and rapid resumption of normal activities after major surgical procedures without an increase in complications or readmissions. It facilitates an early return of bowel function.<sup>1-4</sup> Improved post-operative analgesic techniques and a better understanding

of perioperative care principles with early oral feeding and ambulation have resulted in enhanced post-operative recovery.<sup>5</sup> The purpose of this integrated approach is mainly to reduce the psychological and physiological stresses associated with surgical illness, to reduce tissue catabolism, and enhancing recovery in a rapid way.<sup>6</sup> Many studies have evaluated the effects of standard/conventional care and showed that many of the traditional approaches to surgical care, such as pre-operative bowel clearance, prolonged fasting, prolonged use of nasogastric tubes and drains placed in cavities, enforced bed rest, and the use of graduated diets are unnecessary or even harmful.<sup>7,8</sup>

## Aims

To compare the post-operative recovery rate using ERAS and institutional standard protocol.

## MATERIALS AND METHODS

A prospective case-control study was conducted in Department of General Surgery, Government Rajaji

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Hospital Madurai. Ethics committee approval and informed consent were obtained. Patients from age 10-80 years admitted to general surgical wards with acute abdomen and planned for emergency laparotomy were screened. Patients undergoing re-laparotomies for acute abdomen and presenting with acute abdomen due to trauma are excluded from the study. Patients included in the study were undergone 2 methods of surgical procedure, Group A (Control) with Institutional standard procedure. Group B (Case) undergo ERAS protocol. Patients were randomized using randomization table to undergo recovery protocol. Patient's bowel movement, duration of hospital stay, and pain score were compared between the groups. Data were analyzed using Student's *t*-test in SPSS 11 software.

## RESULTS

A total of 50 patients were recruited, 25 in Group A and 25 in Group B, gender distribution were as follows: There were 14 males and 11 female under cases and 18 males and 7 females under controls. The more patients are in age group 41-50 years (Table 1).

In Group A, patients with duodenal perforation are high (20%) followed by small bowel perforation (16%), Group B - duodenal perforation was high (28%) followed by small bowel perforation and gastric perforation (16%) (Tables 2 and 3).

The mean day of return of bowel function was compared in Groups A and B; Group B was 3.44 days and among the Group A were 4.76. There is a significant difference in the mean day of return of bowel function ( $P < 0.0001$ ) which shows ERAS protocol is better in return of bowel functions (Table 4).

Total days of hospital stay in Group A 10.56 days and Group B 7.88 days. The mean difference of 2.68 with  $P < 0.0001$  shown that Group B is better than Group A (Table 5).

Pain score, Group B shown less pain score than Group A with statistical difference  $P < 0.0001$  (Table 5).

## DISCUSSION

In the study, the patients undergoing emergency laparotomy are subjected to various components of ERAS which involves Pre-operative criteria's like pre-operative counselling, carbohydrate loading, antibiotic prophylaxis, avoidance of mechanical bowel preparation, intraoperative

**Table 1: Distribution of age study patients and study groups**

Age group	Patients	Group A	Group B
10-20	7	6	1
21-30	4	1	3
31-40	11	5	6
41-50	15	7	8
51-60	3	3	0
61-70	8	3	5
71-80	2	0	1

**Table 2: Distribution of diagnosis**

Diagnosis	Group A (%)	Diagnosis	Group B (%)
Abdominal TB	4	Appendicular perforation	8
Appendicular perforation	12	Duodenal perforation	28
Duodenal perforation	20	Gastric perforation	16
Gastric perforation	12	Large bowel gangrene	4
Incision hernia with burst abdomen and bowel prolapse	4	Liver abscess	4
Large bowel perforation	4	Obstructed incisional hernia	8
Ruptured liver abscess	4	Obstructed spigelian hernia	4
Sealed perforation	8	Small bowel gangrene	4
Small and large bowel gangrene	4	Small bowel obstruction	8
Small bowel gangrene	8	Small bowel perforation	16
Small bowel perforation	16		
Uterine perforation	4		

**Table 3: Comparison of days of return of bowel function**

Days of return of bowel function		
Group	Mean±SD	P
Group A	4.76±0.723	<0.0001
Group B	3.44±0.712	

**Table 4: Comparison of days of hospital stay**

Hospital stay		
Group	Mean±SD	P
Group A	10.56±0.821	<0.0001
Group B	7.88±1.764	

**Table 5: Comparison of pain score in study groups**

Pain score		
Group	Mean±SD	P
Group A	3.12±1.2	<0.0001
Group B	2.08±1.07	

and post-operative maintenance of body temperature, post-operative components such as early mobilization, early initiation of diet, early removal of nasogastric tubes, and early removal of abdominal drain's and usage of NSAID's and paracetamol for pain relief and usage of opioid analgesic's only for rescue analgesia.<sup>9-13</sup> A similar analysis was done previously in colorectal and urological surgeries and was found to be effective in enhancing the recovery rate.<sup>14,15</sup> Bowel movement occurs quicker in patients undergone ERAS protocol than the institutional standard when compared with institutional standard protocol which is promising result to restore patient's normal bowel movement.<sup>16</sup> ERAS protocol shown quicker discharge of patients than another group which is shown the similar result in other studies done.<sup>17,18</sup> There is reduction in the pain score compared to control group which is also evident from the other study.<sup>19</sup>

## CONCLUSION

ERAS protocol has shown earlier post-operative recovery rate than institutional standard protocol. Shorter recovery period not only decreases complications/morbidity of the surgery but also reduces the cost of surgery which is a significant factor in patient's point of view.

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# A Study of Effect of Steroids on Post-tonsillectomy Pain in Adults

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## Abstract

**Introduction:** Dexamethasone has been used to reduce the pain in post-operative tonsillectomy. Evidence is there that how much dose to be used to bring this effect.

**Objective:** To compare the efficacy of two different doses of intravenous dexamethasone intraoperatively on pain after tonsillectomy.

**Materials and Methods:** A total of 40 adult patients of age between 18 and 45 years posted for tonsillectomy which was divided into two groups, and different doses of dexamethasone were given and were measured for 7 days at an interval of 6, 12, and 24 h using visual analog scale score.

**Results:** There was significantly no difference between the groups, but the second group of patients required less analgesic agent as compared to the first group.

**Conclusion:** This study shows a slight reduce in pain after use of 20 mg intravenous dexamethasone given intraoperatively while performing electrocautery tonsillectomy. The use of dexamethasone results in small amount of reduction of pain postoperatively, and hence, the use of it benefit and outweighs the risk of this practice.

**Key words:** Dexamethasone, Post-tonsillectomy, Visual analog scale score

## INTRODUCTION

Dexamethasone has been used to reduce the pain in post-operative tonsillectomy. Evidence is there that how much dose to be used to bring this effect. Various studies have been compared using intra- and post-operative use of dexamethasone in children for tonsillectomy.<sup>1-6</sup> The limitations of this study were having a lack of control group, small study group, and invalid pain rating method.

Short-term doses of intraoperative steroids are used routinely by many surgeons especially when operating in the head and neck region, to reduce swelling and protect function. This type of protocol is believed to be safe in otherwise healthy patients.<sup>7-9</sup>

## Dexamethasone

It is a type of steroid medication used in the treatment of many conditions such as rheumatic problems, skin problems, severe allergies, asthma, chronic obstructive lung diseases, croup, and brain swelling.

In preterm labor, it may be used to improve outcomes in the baby. It can be given orally or intravenously or intramuscularly. The effect is seen within a day and lasts for about 3 days.

Long-term use of the drug can cause oral thrush, bone loss, cataracts, muscle weakness, or easy bruising. It also has anti-inflammatory and immunosuppressant effects.

## Post-tonsillectomy

Tonsillectomy is a procedure or surgery to remove tonsils. Nearly, everyone experiences pain after a tonsillectomy. The pain is most often in the throat and frequently in the ears. It gradually decreased with medication and time. Use of dexamethasone can decrease the uses of pain killers and also decreases the swelling of operated part due to its anti-inflammatory effects. Certain complications such

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as bleeding, fever, and dehydration can be seen in post-tonsillectomy patients.

### Visual Analog Scale (VAS) Score

The VAS is a psychometric response scale, which can be used in questionnaires. It is a measurement instrument for subjective characteristics or attitudes that cannot be directly measured.

## MATERIALS AND METHODS

Patients posted for tonsillectomy aged between 18 and 45 years were included in the study. Exclusion criteria were contraindicated for steroid use such as pregnancy, diabetic patients, and psychosis. Exclusion criteria includes contraindications for steroid use such as pregnancy, diabetic patients, psychosis & drug allergies for steroids and lack of cooperation for the study.

Patients were admitted to hospital on the day of operation and remain admitted to hospital for 2 days postoperatively. Pre-operative preparation: Anesthetic induction maintenance & recovery was standardized as per the hospital protocol.

Patients were randomized to receive either 8 mg of dexamethasone or 20 mg of dexamethasone intravenously. Both patient and surgeon were blinded as to which was received.

Tonsillectomy was performed as per standard protocol; 2% lignocaine with 1:200000 adrenalin was injected into tonsillar bed, and then, electrocautery was used to remove the tonsils. Hemostasis was achieved using pressure gauze and cautery.

Each patient was given tramadol nonsteroidal anti-inflammatory drug (NSAID) and paracetamol (PCT), intra and postoperatively. Patients scored their throat pain on VAS. They drew a vertical line of 10 cm where 0 was no pain and 10 was worst pain. As this is a well-accepted, validated method of pain measurement in knowing post-tonsillectomy pain.<sup>10-14</sup>

Analysis was done using Microsoft Excel and SPSS repeated measures were compared using analysis of variance, and non-repeated data were compared using *t*-test.

## RESULTS

About 40 patients were enrolled and 35 of whom returned their data collection forms. 17 were randomized to the placebo group and 18 were randomized to the dexamethasone group.

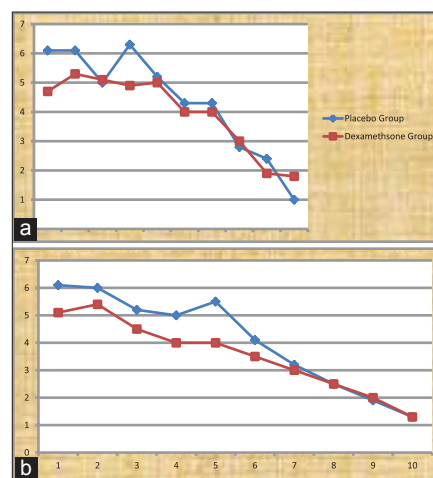
No statistically significant differences between the group of sex, age, smoking status, and reason for tonsillectomy. Pain score is shown in Figure 1. Analysis of variance revealed no significant differences.

The dose of PCT and NSAID is shown in Figure 2, and there were no significant differences between the groups.

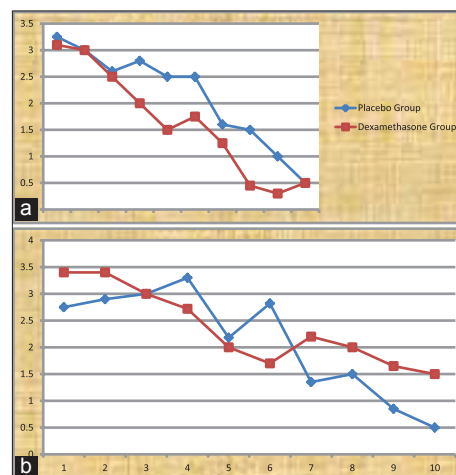
Around 11 patients (32%) in dexamethasone group and 10 patients (29%) in placebo group required no analgesic

**Table 1: Characteristics of study groups**

Characteristics	Placebo group (n=14)	Dexamethasone group (n=15)
Sex		
Male	7	6
Female	7	9
Age, mean, year (range)	27.6 (17.2-52.8)	26.9 (15.5-40.0)
Smokers (n)	7	3
Indication for tonsillectomy (n)		
Recurrent tonsillitis	13	15
Tonsil lesion	1	0



**Figure 1: Comparison of pain score**



**Figure 2: Comparison of analgesic used (PCT & NSAID) in post operatively**

**Table 2: Summary of studies of dexamethasone use in pediatric tonsillectomy**

Study, year	Tonsillectomy method	N	Pain measurement	Steroid dose	Hemorrhagic events, (n)	Significant outcomes
Cafin and Grimes, <sup>1</sup> 1991	SD	S=10 NS=15	Parental questionnaire	8 mg	S=2 NS=1	S=Normal diet sooner
Volk <i>et al.</i> , <sup>2</sup> 1993	SD	S=25 NS=24	Parental questionnaire (scale 0-3)	10 mg	S=2 NS=1	No difference between groups
Ohims <i>et al.</i> , <sup>5</sup> 1995	SD	S=34 NS=35	Faces scale (7 d)	0.5 mg/kg	S=3 NS=0	No difference between groups
April <i>et al.</i> , <sup>4</sup> 1996	EC	S=41 NS=39	Faces and Oucher scales (24 h)	1 mg/kg	S=1 NS=1	No difference in pain between groups; S=Less vomiting, normal diet sooner
Tom <i>et al.</i> , <sup>3</sup> 1996	EC	S=26 NS=32	Parental diary (10 d)	1 mg/kg	S=1 NS=2	S=Less pain, less vomiting, more tolerated normal diet on first day

\*SD: Sharp dissection, EC: Electrocautery, S: Steroid (dexamethasone) group, NS: No steroid (control) group

postoperatively. No significant difference between the groups for time to be able to tolerate normal diet or resume work.

No significant difference between smokers or non-smokers and between male and female found (Tables 1,2).

## DISCUSSION

ENT surgeons use steroids because of anti-inflammatory actions. These are mediated by inhibition of production of inflammatory cell factors resulting in decreased lysosomal enzyme release extravasation of leukocytes and vascular permeability,<sup>9-15</sup> ultimately reducing edema and decreasing fibrosis during healing.

Steroids have many physiological actions, and they exert an effect by binding to specific intracellular receptors that alter gene expression, blocking formation of some substances, and accelerating productions of others.

Well-known side effects include cataracts, avascular necrosis of bone, osteoporosis, hypertension, hyperglycemia, growth disturbances, mood and personality changes, and post-treatment adrenal insufficiency due to suppression.<sup>9</sup>

Dexamethasone is among the most potent glucocorticoids with 36 to 72 h of biological half-life, and it is 25 times as potent as endogenous cortisol.<sup>9</sup> 10 mg of cortisol is secreted by an adult daily which is 0.4 mg of dexamethasone; thus, the dose chosen for study (20 mg) is very supraphysiological. Use of dexamethasone in correct dose for reduction of edema and inflammation in head and neck.<sup>6</sup> Ideally, 1-1.5 mg/kg should be used intravenously.<sup>15</sup>

Steroids reduce the antiemetic effect in oncology patients.<sup>16</sup> In this study, dexamethasone improved pain very slightly, but the use of analgesic decreased after the third day in dexamethasone group.

A significant difference of 2 cm on VAS in initial sample size calculation that was reasonable for biomedical research. Our study suggests that further study of steroid effect in first 12 h after post-tonsillectomy would be challenged. Splinter and Roberts<sup>6</sup> said that vomiting episodes reduced in post-operative cases

## CONCLUSION

This study shows a slight reduce in pain after use of 20 mg intravenous dexamethasone given intraoperatively while performing electrocautery tonsillectomy. The use of dexamethasone results in small amount of reduction of pain postoperatively, and hence, the use of it benefit and outweighs the risk of this practice.

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# Transaxillary Endoscopic Hemithyroidectomy versus Open Hemithyroidectomy for Solitary Thyroid Nodule: A Randomized Study

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## Abstract

**Introduction:** Traditional thyroidectomy technique approaches the thyroid through a transverse incision over the neck. The scar may result in hyperesthesia, restriction of neck movements, and increased patient self-consciousness. Furthermore, in some patients, it can result in hyperplastic or keloid scar formation. Minimally invasive techniques have replaced open surgeries in many surgical fields. Endoscopic transaxillary thyroidectomy is one such minimally invasive technique that may provide superior cosmetic results for patients needing thyroidectomy.

**Materials and Methods:** We did a randomized study comparing endoscopic transaxillary versus traditional open hemithyroidectomy approach in case of a solitary thyroid nodule. We reviewed our series of 57 patients and studied the feasibility and safety of transaxillary endoscopic approach in patients who have undergone hemithyroidectomy between the years 2012 and 2015.

**Results:** The total operative time for the transaxillary endoscopic hemithyroidectomy (TAEHT) is longer compared to the open group. Total operating time was calculated from the time of skin incision to closure. Mean operating time in transaxillary endoscopic group is 132 min and mean operating time in open hemithyroidectomy group is 102.03 min. In comparison, the mean operating time in open hemithyroidectomy is  $45.4 \pm 11.90$ .

**Conclusion:** TAEHT is safe and feasible. However, there is a slight increase in operative time. We also conclude that transaxillary endoscopic thyroidectomy is superior to conventional open hemithyroidectomy in terms of post-operative pain, duration of stay, seroma formation, and cosmesis.

**Key words:** Endoscopic thyroidectomy, Minimally invasive thyroid surgery, Transaxillary thyroidectomy

## INTRODUCTION

Minimally invasive surgeries have replaced open surgeries in many surgical fields. Initiation of laparoscopic cholecystectomy by Reynolds<sup>1</sup> revolutionized the surgical department worldwide. Followed by that, almost all intra-abdominal surgeries were done laparoscopically.

The advantages of surgery performed using minimally invasive techniques in other areas of the body have been well documented. Enhanced cosmesis, optical enhancement, and improved visualization through video magnifications have inspired the use of an endoscopic approach to the thyroid and parathyroid glands as well.

The traditional thyroidectomy technique approaches the thyroid through a transverse incision in the neck. The scar may result in hyperesthesias, restriction of neck movements, and increased patient self-awareness. Furthermore, in some patients of darker skin ethnicity, it can result in hyperplastic and keloid scar formation in a highly visible area of the neck.

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The subject of “endoscopic thyroidectomy” has generated immense interest among thyroid surgeons. Since the first report of endoscopic parathyroidectomy reported by Gagner *et al.*,<sup>2</sup> in 1996, various minimally invasive approaches have been described in the literature for endoscopic thyroidectomy.

The advantages of surgery performed using minimally invasive techniques in other areas of the body have been well documented. Enhanced cosmesis, optical enhancement, and improved visualization through video magnification have inspired the use of an endoscopic approach to the thyroid and parathyroid glands as well.

We did a comparative study between endoscopic transaxillary versus traditional open hemithyroidectomy approach in case of solitary thyroid nodules. We reviewed our series and studied the feasibility and safety of transaxillary endoscopic approach in patients who have undergone hemithyroidectomy.

## MATERIALS AND METHODS

All patients undergoing hemithyroidectomy (open and minimally invasive) for solitary thyroid nodules for 3 years in the Department of General Surgery, Sri Ramachandra University, were included in the study.

All benign solitary thyroid nodules of size 5 cm or less, as confirmed by ultrasonography (USG) and fine-needle aspiration cytology (FNAC), in patients 18 years or above of age were included in the study. Malignant, recurrent nodules, and patients with American Society of Anaesthesiologists >3 were excluded from the study.

All the patients underwent thorough clinical examination after registration. Hematological (complete blood count) and biochemical (random blood sugar, renal function test, and serum electrolytes) evaluation, Skiagram neck (antero-posterior and lateral view), thyroid function tests, and coagulation profile were done for all cases. Electrocardiogram was done for those who were above 40 years.

All the patients were subjected to indirect laryngoscopy done by otorhinolaryngologists. All patients included in the study were subjected to FNAC and USG neck.

All 57 patients included in the study were subjected to one of the surgeries mentioned earlier. Of the 57 patients, 26 underwent transaxillary endoscopic hemithyroidectomy (TAEHT), and 31 patients underwent traditional open thyroidectomy selected randomly. 12F suction drain was

placed in both groups. The following parameters were compared between both groups. Duration of surgery was documented in all cases. Post-operative pain score was recorded on post-operative day (POD) 1, 3, and 7 using visual analog scale.

Post-operative drain, seroma, recurrent laryngeal nerve (RLN) damage, and duration of hospital stay were also studied. Patients' post-operative histopathology reports were taken into consideration.

## RESULTS

The various parameters were recorded in Tables 1-8.

**Table 1: Age**

Group	N	Mean	Standard deviation	Standard error mean
Open	31	31.38	7.481	1.230
TAEHT	26	29.00	6.190	1.214

TAEHT: Transaxillary endoscopic hemithyroidectomy

**Table 2: Sex (Male: Female)**

Sex	Open	TAEHT	Total
Male	2	1	3
Female	29	25	55

TAEHT: Transaxillary endoscopic hemithyroidectomy.

**Table 3: Duration of surgery**

Group	N	Mean (min)	Standard deviation	Standard error mean
Open	31	102.03	16.093	2.646
TAEHT	26	132.65	7.445	1.460

TAEHT: Transaxillary endoscopic hemithyroidectomy

**Table 4: Post-operative day 1**

Group	N	Mean	Standard deviation	Standard error mean
Open	31	3.38	0.594	0.098
TAEHT	26	2.00	0.0001	0.0001

TAEHT: Transaxillary endoscopic hemithyroidectomy

**Table 5: Post-operative day 3**

Group	N	Mean	Standard deviation	Standard error mean
Open	31	2.57	0.603	0.099
TAEHT	26	1.00	0.0001	0.0001

TAEHT: Transaxillary endoscopic hemithyroidectomy

**Table 6: Post-operative day 7**

Group	N	Mean	Standard deviation	Standard error mean
Open	31	1.27	0.450	0.074
TAEHT	26	0.20	0.408	0.082

TAEHT: Transaxillary endoscopic hemithyroidectomy

**Table 7: Duration of hospital stay**

Group	N	Mean (days)	Standard deviation	Standard error mean
Open	31	3.84	0.646	0.106
TAEHT	26	2.42	0.643	0.126

TAEHT: Transaxillary endoscopic hemithyroidectomy

**Table 8: Post-operative drain**

Group	N	Mean (ml)	Standard deviation	Standard error mean
Open	31	19.46	10.235	1.683
TAEHT	26	13.42	6.760	1.326

TAEHT: Transaxillary endoscopic hemithyroidectomy

## DISCUSSION

Benign thyroid nodules can be treated by various modalities. The main objective for minimally invasive thyroid surgeries in all studies is cosmesis, lesser pain, and lower/equal morbidity compared to the open approach. A meta-analysis study done by Chen *et al* showed that minimally invasive thyroid surgeries have improved outcomes in terms of pressure symptoms and cosmesis when compared to other modalities.<sup>3</sup> We did a comparative study between conventional open hemithyroidectomy and TAEHT in terms of cosmesis, post-operative pain, duration of stay, duration of surgery, and complications. We have compared our observation with the studies conducted by Feilin *et al.* and Bhargav *et al.*

Study done by Feilin *et al.*<sup>4</sup> was a comparative study, in which endoscopic thyroidectomy was done through breast approach. They included both hemithyroidectomy as well as total thyroidectomy in their study whereas the present study compares only hemithyroidectomy. They use CO<sub>2</sub> insufflation to maintain the working space in endoscopic thyroidectomy group similar to the present study. A study done by Bhargav *et al.*<sup>5</sup> evaluated the feasibility and safety of single-incision TAEHT without using CO<sub>2</sub> insufflation. They included both hemithyroidectomy as well as total thyroidectomy, wherein total thyroidectomy, the other side is approached through the contralateral axilla. In this study, we have excluded malignant or recurrent nodule and size of the nodule >5 cm. This exclusion criterion is similar to the studies mentioned above.

The age of the patients in present study varies in a range from 21 to 45 years. Mean age was 31.38 years in conventional open hemithyroidectomy group and it was 29 years in TAEHT group. This is comparable with the studies mentioned above.

Female: Male ratio in the present study was 4:1. The majority of the patients were females, which correlates with the other studies reviewed. Female:Male ratio 14:2 in study done by Bhargav *et al.*<sup>5</sup>

The main interest of present study as mentioned before was to compare the TAEHT versus open hemithyroidectomy in terms of duration of surgery, post-operative pain, complications, and cosmetic outcome.

The total operative time for the TAEHT is longer compared to the open group. Total operating time was calculated from the time of skin incision to closure. Mean operating time in transaxillary endoscopic group is 132 min, and mean operating time in open hemithyroidectomy group is 102.03 min. In comparison, the mean operating time in open hemithyroidectomy is  $45.4 \pm 11.90$  versus  $79.9 \pm 20.10$  min in endoscopic hemithyroidectomy in a study done by Feilin *et al.*<sup>4</sup> The mean operative time in the study done by Bhargav *et al.*<sup>5</sup> is 123.4 min. In Gagner<sup>2</sup> study, mean operative time for his anterior cervical approach is 220 min.

There was no conversion to open in the endoscopic thyroidectomy group. On comparison, there is no conversion in other studies noted as well.

RLN was identified in all cases in both open and endoscopic group. Endoscopic approach provides better, magnified views of the RLN and the parathyroid gland resulting in fewer complications.

Post-operative drain amount is quantified in both open and endoscopic groups. 12F suction drain is placed in both groups. Drain is removed on POD 2 in both groups. Mean drain amount in open group is 19.46 ml, whereas in transaxillary endoscopic group is 13.42 ml. The study by Bhargav *et al.*<sup>5</sup> states that there was prolonged drainage (5.4 days) postoperatively, which again increases the hospital stay. This is due to extensive dissection due to gasless technique, which is restricted in our technique due to gas insufflation.

Mean duration of stay in open hemithyroidectomy group is 3.84 days, whereas, in transaxillary endoscopic thyroidectomy group, it is 2.42 days. There is a significant reduction in duration of stay. Mean duration of stay is 5.3 days in a study done by Bhargav *et al.*<sup>5</sup> whereas, in a study done by Chantawibul *et al.*,<sup>6</sup> duration of stay is 2.9 days.

There is a significant reduction in post-operative pain in TAEHT as compared to the open group. Pain score is documented on POD 1, 3, and 7 using visual analog scale.

Once post-operative wound collection occurs, the options are continued observation in the hope of gradual spontaneous resolution, needle aspiration, and evacuation of wound collection under local or general anesthesia. Collections that occur in the immediate post-operative period are due to continued or delayed bleeding from

the wound. At this stage, usually surgical intervention is required unless the bleeding is minimal. Later in the post-operative course, tissue fluid can collect in the operated area and give rise to a seroma. This can be aspirated with a needle or observed without any intervention. We record it as seroma if there is intervention done for it to reduce.

Seroma formation post drain removal was noted more in open thyroidectomy. Some studies quote that the extensive dissection in the transaxillary approach leads to more seroma formation. This depends on whether CO<sub>2</sub> insufflation is used or not. The use of CO<sub>2</sub> provides good operating space, hence reducing the amount of dissection. Insertion of only the working ports and minimal dissection greatly minimized the amount dissection on our patients and the incidence of seroma formation was nil.

In conventional open approach, the gland is reached through a range of variably sized collar neck incisions in the neck, which can result in a scar with hyperesthesia, paresthesia, and increased patient self-awareness. Furthermore, keloid or hypertrophic scar worsens the cosmetic outcome, especially in dark-skinned individuals. Restriction of neck movements and some amount of dysphagia is also noted in some patients undergoing open hemithyroidectomy.

The transaxillary approach utilizes an access through the axilla, thus avoiding a cervical or chest wall incision. This is especially true in the case of benign thyroid nodules, which is common in the young female population. Patients who underwent transaxillary endoscopic thyroidectomy were

extremely satisfied with the scar in the axilla compared to the conventional open group. The subsequent scar is hidden in the axilla and remains under clothing. If the patient is prone to hypertrophic scar formation, the final scar will be well hidden within the axilla and quite amenable to scar modification.

## CONCLUSION

In this study, we conclude that TAEHT is safe and feasible. However, there is a slight increase in operative time. We also conclude that transaxillary endoscopic thyroidectomy is superior to conventional open hemithyroidectomy in terms of post-operative pain, duration of stay, seroma formation, and cosmesis.

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# Comparing Fixation versus Non-fixation of Mesh in Laparoscopic Totally Extraperitoneal Repair of Inguinal Hernia: A Prospective Study

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## Abstract

**Introduction:** Inguinal hernia repair is one of the most common surgical procedures done worldwide. Conventional repair involves the usage of a mesh to cover the hernia defect to prevent recurrence. The mesh is fixed securely without tension in open hernia repair. Laparoscopic surgery for inguinal hernia repair is done by two methods, which only vary in approach to the preperitoneal space. They include laparoscopic transabdominal preperitoneal inguinal hernia repair and totally extraperitoneal (TEP) inguinal hernia repair.

**Purpose:** The purpose of this study is to compare the outcomes and complications between fixation using suture and non-fixation of mesh in laparoscopic TEP inguinal hernia repair.

**Materials and Methods:** The study period was 1 year, and all patients were followed up for a period of 1 year following surgery. All the surgeries were performed by a single surgeon, and all the ultrasounds were performed by the same radiologist.

**Results:** The study population was randomized into two groups, 46 patients met with the inclusion criteria and were included in the study. Of the 46 patients, 22 patients were randomized to the group in whom, the mesh was fixed. 24 patients were randomized to the group in which the mesh was not fixed. Out of 46 patients, 36 had unilateral hernia and 10 had bilateral hernia giving a total sample size of 56. Out of 36 patients who had unilateral hernia, 11 had hernia on left side. 25 had hernia on the right side.

**Conclusion:** We conclude that the placement of mesh without fixation results in less post-operative pain, consumes less time for placement of mesh and is cost-effective in comparison to mesh fixation technique. And there is no significant difference in the mesh migration in our study.

**Key words:** Laparoscopic inguinal hernia repair, Mesh migration, Non fixation of mesh, Totally extraperitoneal

## INTRODUCTION

Totally extraperitoneal (TEP) inguinal hernia repair was first described in 1993 by McKernon and Laws. Laparoscopic inguinal hernia repair has many advantages over open

repairs such as less post-operative pain, early return to daily activities and to work, lesser incidence of neurogenic pain, bleeding, infection, and seroma. Laparoscopic inguinal hernia repair is similar to the concept of inguinal hernia repair proposed by Stoppa.

During laparoscopic surgery, the mesh is generally placed and sutured using suture materials or using fixation devices such as staples, tacks, or tissue glue. Stapling can cause scarring and pain at the staple sites. The purpose of this study is to compare the outcomes and complications of non-fixation of mesh in laparoscopic TEP inguinal hernia repair.

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## MATERIALS AND METHODS

### Inclusion Criteria

Patients that were more than 18 years of age, who were willing to participate and provided informed consent, were included in the study. Patients diagnosed clinically with direct and indirect inguinal herniae, unilateral, and bi-lateral inguinal herniae were included in the study.

### Exclusion Criteria

Patients that were unfit for general anesthesia, who were diagnosed to have complicated inguinal herniae such as strangulated and obstructed hernia, were excluded from the study.

They were prospectively randomized by closed envelope method into two groups, one of which underwent laparoscopic TEP inguinal hernia repair with a polypropylene mesh fixed with 2-0 prolene and the other groups underwent surgery without the mesh being fixed.

A 12 cm × 15 cm polypropylene, monofilament, non-absorbable mesh that weighed 80 g/m<sup>2</sup> and had a thickness of 0.50 mm and pore size of 0.5 mm × 0.7 mm was used for all patients.

The study period was 1 year, and all patients were followed up for a period of 1 year following surgery. All the surgeries were performed by a single surgeon, and all the ultrasounds were performed by the same radiologist.

### Ultrasonography

Serial ultra-sonogram analysis of patient was done preoperatively, on post-operative day 1 (POD 1) (Visit 1), on POD 7-9 (Visit 2), and after 6 months (Visit 3) post-operatively. The distance of lateral border of mesh to anterior superior iliac spine was taken as "A," the distance of pubic symphysis to medial border of mesh as "B" and the superior border of mesh to a point of intersection of two imaginary lines, one drawn horizontally through the level of umbilicus and the second drawn vertically up through the mid-inguinal point was taken as "C" were measured on Visit 1, 2 and 3.

Measurement of pain score was done using visual analog scale (VAS score) and a score between 0 and 10 was recorded: 0 - no pain, 1-3 - mild pain, 4-6 - moderate pain, and 7-10 - severe pain. These measurements were taken on Visit 0 - the day of surgery (6 h after surgery), Visit 1, 2 and 3 (Table 2-9).

### Statistical Analysis

The statistical analysis for this study was performed using SPSS software version 15 for windows. A value of  $P <$

0.05 was chosen as the significance level for outcome measures.

The analysis was done for paired  $t$ -test. Continuous variables are expressed as means or medians and were compared using  $t$ -tests, analysis of variance, or Mann-Whitney U-tests as appropriate. Categorical variables are expressed as proportions and were compared using either  $\chi^2$  or Fisher exact tests. A 2-sided  $P < 0.05$  was considered statistically significant.

### Statistical Data

- Total number of patients – 46
- Total number of unilateral hernia - 36
- Total number of bilateral hernia – 10
- Sample size - 56 [36+(10×2)]
- Mesh fixed in - 32
- Mesh was not fixed in - 24.

## RESULTS

The study population was randomized into two groups, 46 patients met with the inclusion criteria and were included into the study. Of the 46 patients, 22 patients were randomized to the group in whom, the mesh was fixed. 24 patients were randomized to the group in which the mesh was not fixed. Out of 46 patients, 36 had unilateral hernia and 10 had bilateral hernia giving a total sample size of 56. Out of 36 patients who had unilateral hernia, 11 had hernia on left side. 25 had hernia on the right side.

### Mesh Migration

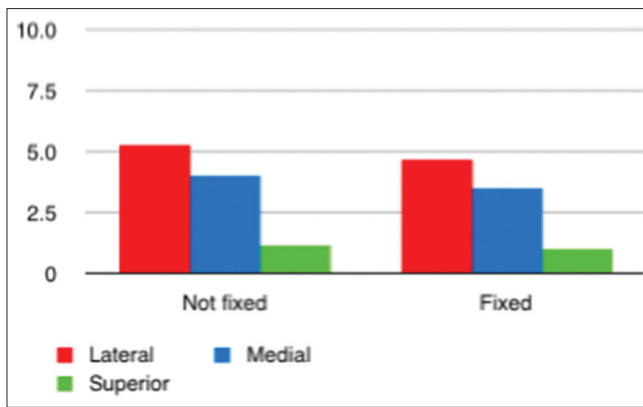
There is minimal movement of mesh in both groups, the group with mesh unfixed showing average movement of 5.31 mm, 4.04 mm and 1.21 mm in lateral, medial and superior directions, respectively. The group with mesh fixation showed average movement of about 4.69 mm, 3.56 mm and 1.02 along lateral, medial and superior directions, respectively. On comparing the values, movement of mesh in group with no fixation was little more than the fixation group. However, the results were not statistically significant. Hence, we conclude that there is negligible mesh migration Table 1 and Graph 1.

### P Value for Mesh Migration

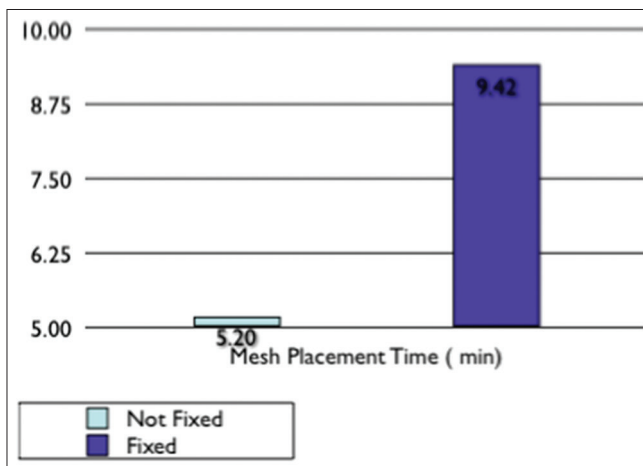
- P value for fixed group - 0.217
- P value for non-fixed group - 0.433. Significant  $P > 0.5$ .

### Time Taken for Mesh Placement

- Average time for mesh fixation
- Average time taken for placement of mesh without fixation - 5 min 20 s



Graph 1: Movement of mesh (in mm)



Graph 2: Time taken for mesh fixation

- Average time taken for placement of mesh with fixation - 9 min 42 s (Graph 2).

### Hernia Recurrence

All patients were followed up for a period of 1 year, and there were no patients with signs and symptoms suggestive of recurrence of inguinal hernia postoperatively.

### Post-operative Pain

Post-operative pain was measured using VAS score; we did not find any difference in pain score between groups on the day of surgery, but there is a statistically significant difference on Visit 1 (POD 1). Average pain score for fixed - 1.73 and unfixed - 1.13. All patients irrespective of the groups did not suffer any pain on Visit 2 and Visit 3 (Table 8 and 9).

## DISCUSSION

In our study, we included patients who were more than 18 years of age and were diagnosed with unilateral/bilateral inguinal herniae which were direct/indirect or both.

Table 1: Movement of mesh (in mm)

Group	Lateral (mm)	Medial (mm)	Superior (mm)
Not fixed	5.31	4.04	1.21
Fixed	4.69	3.56	1.02

Table 2: Group statistics

Mesh	N	Mean	Standard deviation	Standard error of mean
V1A				
Fixed	32	31.009	7.7735	1.3742
Not fixed	24	32.871	6.7654	1.3810
V3A				
Fixed	32	30.54	7.602	1.344
Not fixed	24	32.34	7.193	1.468

All the procedures (TEP) were standardized. The pre-peritoneal space was created by open technique and blunt dissection of the space was done by the telescope and subsequent insufflation with carbon dioxide, compared to many who advocate the use of balloons. We found that our technique was cost-effective with no difficulty encountered in space creation. The hernial sac is it direct or indirect was completely dissected down up to the point where the vas deferens turns medially.

We placed a 12 × 15 cm mono-filament, non-absorbable polypropylene mesh for both groups. In one group, we placed the mesh without fixation and in another group; we fixed the mesh in two places, viz., Cooper's ligament (medially) and anterior abdominal wall (laterally).

The transversalis fascia, rectus muscle, Cooper's ligament, and the pubic bone have emerged as the traditional safe points of fixation with avoidance of infero medial and inferolateral anchorage that is fraught with dangerous complications according to Parshad *et al.*<sup>1</sup>

Non-fixation of the mesh is based on a principle that when intra-peritoneal pressure is evenly distributed over the large peritoneal surface from the inside the mesh is kept in place without need for fixation as explained by Deerenberg *et al.*

### Mesh Migration

Jamadar *et al.*<sup>2</sup> have experience in using sonography to study the mesh and its behavior in abdominal wall herniae. The mesh most commonly appears as a linear echogenic interface with posterior acoustic shadowing. The mesh is differentiated from adjacent structures by its superficial location and absence of peristalsis which helps in differentiating it from bowel.

**Table 3: Independent samples test**

Group	Levene's test for equality of variances		t-test for equality of means						
	F	Sig.	t	df	Sig. (2-tailed)	Mean difference	Standard error difference	95% confidence interval of the difference	
								Lower	Upper
V1A									
Equal variances assumed	0.004	0.952	-0.936	54	0.353	-1.8615	1.9877	-5.8466	2.1237
Equal variances not assumed			-0.955	52.737	0.344	-1.8615	1.9482	-5.7695	2.0466
V3A									
Equal variances assumed	0.086	0.771	-0.896	54	0.374	-1.798	2.007	-5.821	2.225
Equal variances not assumed			-0.903	51.079	0.371	-1.798	1.990	-5.794	2.198

T: Test for lateral movement; V1A -distance between anterior superior iliac spine to lateral border of mesh on Visit 1; V3A: Distance between anterior superior iliac, spine to lateral border of mesh on Visit 3

**Table 4: Group statistics**

Mesh	N	Mean	Standard deviation	Standard error of mean
V1B				
Fixed	32	16.300	7.1414	1.2624
Not fixed	24	18.504	8.4278	1.7203
V3B				
Fixed	32	16.656	6.6037	1.1674
Not fixed	24	16.800	5.5661	1.1362

**Table 5: Independent samples test**

Group	Levene's test for equality of variances		t-test for equality of means						
	F	Sig.	t	df	Sig. (2-tailed)	Mean difference	Standard error difference	95% confidence interval of the difference	
								Lower	Upper
V1B									
Equal variances assumed	0.000	0.984	-1.058	54	0.295	-2.2042	2.0835	-6.3812	1.9729
Equal variances not assumed			-1.033	44.802	0.307	-2.2042	2.1338	-6.5025	2.0941
V3B									
Equal variances assumed	0.875	0.354	-0.086	54	0.932	-0.1437	1.6696	-3.4912	3.2037
Equal variances not assumed			-0.088	53.203	0.930	-0.1437	1.6290	-3.4108	3.1233

T: Test for medial movement; V1B: Distance between Pubic Symphysis to medial border of mesh on Visit 1; V3B: Distance between Pubic Symphysis to medial border of mesh on Visit 3

**Table 6: Group statistics**

Mesh	N	Mean	Standard deviation	Standard error of mean
V1C				
Fixed	32	53.234	3.1676	0.5600
Not fixed	24	52.675	1.3895	0.2836
V3C				
Fixed	32	52.167	3.2032	0.5662
Not fixed	24	52.796	1.4141	0.2886

According to Crespi *et al.*,<sup>3</sup> sonography is better in identifying mesh than computed tomography in patients with polypropylene mesh who had undergone inguinal hernioplasty.

### Hernia Recurrence

In our study, we evaluated our patients till 1 year after surgery and did not find any signs or symptoms suggestive

of recurrence for any of our patients during the entire course of the study. In general, any recurrence occurring within 6 months of surgery indicates technical failure.

Liem *et al.*<sup>4</sup> elucidate that majority of recurrences following TEP happens in the first year after surgery and are always due to surgeon related factor of either mesh migration or displacement. This is precisely the reason we need to

**Table 7: Independent samples test**

Group	Levene's test for equality of variances		t-test for equality of means						
	F	Sig.	t	df	Sig. (2-tailed)	Mean difference	Standard error difference	95% confidence interval of the difference	
								Lower	Upper
V1C									
Equal variances assumed	8.796	0.004	0.807	54	0.423	0.5594	0.6928	0.8296	1.9483
Equal variances not assumed			0.891	44.959	0.378	0.5594	0.6277	-0.7049	1.8236
V3C									
Equal variances assumed	9.026	0.004	-0.897	54	0.374	-0.6290	0.7011	-2.0347	0.7767
Equal variances not assumed			-0.990	45.099	0.328	-0.6290	0.6356	-1.9090	0.6511

T: Test for vertical movement; V1C - distance between superior border of mesh to a point of intersection of two imaginary lines, one drawn horizontally through the level of umbilicus and the second drawn vertically up through the mid inguinal point on Visit 1; V3C - distance between superior border of mesh to a point of intersection of two imaginary lines, one drawn horizontally through the level of umbilicus and the second drawn vertically up through the mid inguinal point on Visit 3

**Table 8: Group statistics**

Mesh	N	Mean	Standard deviation	Standard error of mean
VAS 0				
Fixed	22	2.91	0.294	0.063
Not fixed	24	2.79	0.415	0.085
VAS 1				
Fixed	22	1.73	0.550	0.177
Not fixed	24	1.13	0.680	0.139
VAS 2				
Fixed	22	0.00	0.000 <sup>a</sup>	0.000
Not fixed	24	0.00	0.000 <sup>a</sup>	0.000
VAS 3				
Fixed	22	0.00	0.000 <sup>a</sup>	0.000
Not fixed	24	0.00	0.000 <sup>a</sup>	0.000

<sup>a</sup>t cannot be computed because the standard deviations of both groups are 0

**Table 9: Independent samples test**

Group	Levene's test for equality of variances		t-test for equality of means						
	F	Sig.	t	df	Sig. (2-tailed)	Mean difference	Standard error difference	95% confidence interval of the difference	
								Lower	Upper
VAS 0									
Equal variances assumed	5.335	0.026	1.098	44	0.278	0.117	0.107	-0.098	0.333
Equal variances not assumed			1.114	41.487	0.272	0.117	0.105	-0.095	0.330
VAS 1									
Equal variances assumed	0.585	0.448	3.284	44	0.002	0.602	0.183	0.233	0.972
Equal variances not assumed			3.314	43.371	0.002	0.602	0.182	0.236	0.969

figure out whether fixing or not fixing the mesh makes any difference to these factors. The same point was highlighted by Parshad *et al.*<sup>1</sup> What we are trying to achieve in our study is to bring about a quantitative and objective assessment with respect to mesh migration.

Davis and Arregui<sup>5</sup> recommend that a mesh of size 10 cm × 15 cm is sufficient for laparoscopic hernia repairs without fixation.

Taylor *et al.*<sup>6</sup> stated that they had one recurrence in the fixated group (1/247) whilst none in the unfixated group. Fixation increased operative costs by approximately 340\$ US. They conclude that mesh fixation in TEP is associated with increased operative cost and chronic pain

Koch *et al.*<sup>7</sup> stated that eliminating fixation does not lead to increase in rate of recurrence. They recommend placement of mesh without fixation for hernia defect <3 cm.

### Post-operative Pain

In our study, patients reported mild pain which corresponded to a VAS score of 3 or 2 on the day of surgery after about 6 h immediately after surgery, but the pain reduced significantly at 24 h post-surgery. Almost all of them returned to normal activities on POD 1. There was no difference in pain in the fixed or non-fixed group.

Ferzli *et al.*<sup>8</sup> states that there were no significant difference in pain between fixation and non-fixation group for a 12-month follow-up period. They added that fixation presents an inherent risk of nerve damage.

Burcharth *et al.*<sup>9</sup> say the descriptive and quantitative equivalence with VAS is an accepted system of measurement.

Koch *et al.*<sup>7</sup> state that foregoing the need for fixation, reduces the necessity and use of post-operative narcotic analgesic, results in reduction in length of hospital stay and lessens the probability of developing urinary retention postoperatively. It does not lead to significant reduction in post-operative pain.

Beattie *et al.*<sup>10</sup> have concluded that post-operative pain after mesh fixation in laparoscopic hernia repair is due to injury of genitofemoral nerve.

We infer that non-fixation of mesh is safe alternative to fixation, considering the cost effectiveness, and ease of the technique.

### CONCLUSION

The outcomes of techniques of mesh fixation over non-fixation of mesh were studied in respect to mesh migration, hernia recurrence, time of mesh placement, and post-operative pain.

#### 1. Mesh migration

In both groups, there was no statistically significant mesh migration.

#### 2. Hernia recurrence

The patients were monitored for 1 year postoperatively on a regular basis. There were no cases of clinically evident hernia recurrence

#### 3. Time taken for mesh placement

The average time taken for mesh placement with fixation was longer than non-fixation.

#### 4. Post-operative pain

Fixation of mesh showed significantly more pain on POD “1” compared to non-fixation. However, there was no difference in pain between both groups on POD “7.”

Hence, we conclude that the technique of mesh fixation is NOT superior for prevention of mesh migration and hernia recurrence.

We also conclude that the placement of mesh without fixation results in less post-operative pain consumes less time for mesh placement and is cost-effective in comparison to mesh fixation technique.

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# Perinatal Mortality: Does Antenatal Care Matters? A Retrospective Analysis

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## Abstract

**Introduction:** Perinatal mortality rate (PMR) is the most sensitive index of the health status of women and quality of maternal and child health services. Over 130 million babies are born every year, large numbers of children die soon after birth, many of them in the first 4 weeks of life (neonatal deaths) and most of them in the first week (early neonatal deaths).

**Objective:** The objective of this study was to find out the prevalence of perinatal mortality and the factors associated with perinatal death.

**Methods:** A retrospective analysis was done in a tertiary care center. All perinatal deaths during the period between January and December 2015 were included in the study.

**Results:** There were 6722 deliveries and 256 perinatal deaths during the study period. PMR was 37.2/1000 births. The stillbirth rate was 26.2/1000 births, and early neonatal death rate was 11.06/1000 births. Severe pre-eclampsia/eclampsia and antepartum hemorrhage (APH) were the common causes of perinatal deaths. Of concern, we found more percent of unbooked cases associated to stillbirth (119 vs. 61) with severe pre-eclampsia/eclampsia, APH, and undetermined causes were main factors related to stillbirth death.

**Conclusion:** Poor antenatal care was found associated with increased PMR. Hypertension and APH are leading causes of perinatal deaths. The majority of these complications occur in the later part of pregnancy, increased vigilance during antenatal care at the base level can reduce these deaths.

**Key words:** Antenatal care, Causes, Perinatal deaths, Tertiary care center

## INTRODUCTION

Perinatal mortality rate (PMR) is the most sensitive index of the health status of women and quality of maternal and child health services. Over 130 million babies are born every year, large number of newborns die soon after birth, many of them in the first 4 weeks of life (neonatal deaths) and most of them in the first week (early neonatal deaths). For every baby who dies in the first week after birth, another

is born dead (fetal deaths/stillbirths). More than 98% of the estimated 3.7 million neonatal deaths and 3.2 million stillbirths per year occur in the developing countries.<sup>1</sup>

For international comparison, 1000 g and/or 28 weeks gestation is recommended. The global estimation of PMR is 10/1000 births in developed countries, 50/1000 births in developing countries, and 60/1000 births in least developed countries.<sup>2</sup> According to the WHO, global perinatal estimates for the year 2000 for India is 70, one-third of stillbirths occur during delivery.<sup>3</sup> The PMR (2005-2006) in India is 49/1000 births as per the WHO.<sup>4</sup> Although this decrease is evident even in India, perinatal mortality is still high as compared to developed countries.

Ensuring that the labor and the first 24 h postpartum are managed by a skilled care provider is one of the keys to

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achieving this aim.<sup>5</sup> Measures of perinatal mortality can be derived using data from vital statistics, routine health services data, or sample surveys. However, in developing countries, incomplete registration of the births and deaths results in inaccurate vital statistics.<sup>6</sup> Reduction in the perinatal mortality requires community-based interventions in combination with more advanced facilities, technology, and skilled human resources.<sup>7,8</sup> The present study aims to find out the causes in our institute and detect further possible measures to reduce the mortality.

## MATERIALS AND METHODS

The study is a retrospective analysis of all deliveries conducted at the Niloufer Hospital, Osmania Medical College from January 2015 to December 2015. All perinatal deaths, i.e. stillbirths and early neonatal deaths were analyzed in detail. Pregnant women having at least three antenatal visits were considered as booked cases while others were taken as unbooked cases. Parameters studied include age, parity, booked or unbooked, different causes of deaths including antepartum, intrapartum and early neonatal death, birthweight as well as gestational age.

Stillbirth defined as fetal death more than or equal to 28 weeks gestation or more than 1000 g and early neonatal death defined as death occurring in the first 7 days of birth. PMR was calculated by stillbirths plus early neonatal death per 1000 total births.

The data obtained were tabulated and analyzed using rates, ratios, and percentages.

## RESULTS

There were a total of 256 perinatal deaths out of 6869 births during the study period giving a PMR of 37.2, stillbirth rate 26.2, and early neonatal mortality rate of 11.06/1000 births as shown in Table 1. There were 256 perinatal deaths, of which, 9 (3.51%) had multiple pregnancy. Delivery was conducted vaginally in vertex presentation in 204 births (79.6%), assisted breech delivery in 5 (1.95%), and cesarean section in 38 births (14.84%).

Out of 256 deaths, 180 (70.31%) were unregistered. According to gestational age, most of the perinatal deaths were in preterm (57%) than terms. Perinatal mortality was highest in low birthweight babies (<2500 g). The maximum perinatal death was seen in 20-30 years age group and primigravida constituted maximum perinatal deaths (Table 2).

Most of the perinatal deaths were due to severe pre-eclampsia, antepartum hemorrhage (APH), and prematurity

**Table 1: Perinatal index**

Characteristics	Booked	Unbooked	Total
Total births	5768	954	6722
Antepartum deaths	47	104	151
Intrapartum deaths	14	15	29
Early neonatal deaths	15	61	76
Stillbirths (Ante partum+Intra partum)	61	119	180
Perinatal deaths	76	180	256
Perinatal mortality rate (PMR) per 1000 births	11.0	26.2	37.2
Stillbirth rate per 1000 births	8.88	17.32	26.20
Early neonatal death rate per 1000 live births	2.18	8.88	11.06

**Table 2: Demographic variables and perinatal mortality**

Demographic variables	Total births	Perinatal deaths (%)
Gestational age (weeks)		
28≤32	152	58 (22.65)
32≤37	587	88 (34.37)
37≤42	5934	110 (42.96)
≥42	9	0 (0)
Birthweight (g)		
500≤1000	108	22 (8.59)
1000≤1500	231	98 (38.28)
1500≤2500	2289	90 (35.15)
>2500	4231	46 (17.96)
Age in years		
10≤20		20 (7.8)
20≤30		208 (81.2)
30≤40		25 (9.7)
≥40		3 (1.17)
Parity		
Primi		129 (50.39)
G2		59 (23.04)
G3		49 (19.14)
G4		11 (4.29)
≥G5		8 (3.12)

mainly. However, the cause was undetermined in 37 cases (14.4%) (Table 3).

## DISCUSSION

Niloufer Hospital for Women and Children is a tertiary care teaching hospital that receives several high-risk pregnancies in the state of Telangana and adjoining states of Maharashtra, Andhra Pradesh, and Karnataka. Most of them are transported without proper stabilization from referral hospitals. Hospital-based data on perinatal mortality are not truly representative of the community at large because the data often pertain to selective population of high-risk mothers.<sup>9</sup>

The PMR in our study is 37.2/1000 births. In booked cases, it is only 11.0 compared to 26.2 in unbooked cases which is comparable with other studies.<sup>10-13</sup> This was expected as the

**Table 3: Showing different causes of deaths**

Causes	Stillbirth (AP+IP)*	Early neonatal death	Total death (n=256) (%)
Severe pre-eclampsia and eclampsia	35	22	57 (22.2)
APH	35	15	50 (19.5)
Undetermined	28	9	37 (14.4)
Prematurity	16	21	37 (14.4)
Oligohydramnios	15	1	16 (6.25)
IUGR	12	2	14 (5.4)
Congenital anomaly	13	0	13 (5.07)
Multiple pregnancy	9	0	9 (3.5)
Birth asphyxia	7	1	8 (3.1)
MAS	3	2	5 (1.95)
Severe anemia	3	1	4 (1.56)
Gestational diabetes	2	1	3 (1.17)
Infections	2	0	2 (0.78)
Cord prolapsed and cord problems	0	1	1 (0.39)

\*AP: Antepartum hemorrhage, IP: Intrapartum hemorrhage, MAS: Meconium aspiration syndrome, IUGR: Intrauterine growth restriction, APH: Antepartum hemorrhage

study was carried out in tertiary care hospital where many of the pregnant women are referred from the peripheral hospitals because of high-risk pregnancy. Stillbirth rate in the study is 26.2/1000 births. The rate is higher in unbooked cases (17.32 vs. 8.88/1000 births). The early neonatal rate is only 11.06/1000 live births. More perinatal deaths occurred in patients not receiving antenatal care, and these are consistent with following studies.<sup>10-12,14,15</sup>

Perinatal deaths were more in primigravida compared to multigravida were similar noted in other studies.<sup>12,16,17</sup> The PMR is more in lower gestational age and births weight.<sup>10,11,13,14</sup> Preterm labor has been the subject of research for many years. The major causes are pre-eclampsia or eclampsia, APH, prematurity, oligohydramnios, intrauterine growth restriction (IUGR), congenital anomaly, and cord problems. Undetermined group still constitutes about 14.4% of the perinatal deaths. Fetal autopsy may help to determine some of the causes. Antenatal steroids and up gradation of the neonatal set up will further decrease deaths. Pre-eclampsia/eclampsia accounted for 22.2% of deaths but mostly related to lack of proper antenatal care with poor nutrition. APH can be anticipated to some extent by early localization of placenta by ultrasonography. Severe pre-eclampsia/pre-eclampsia and APH were the important causes of the perinatal deaths; similar findings were noted in other studies<sup>10-14</sup>. Congenital abnormality also accounted for 5.07%. Routine screening programs and expensive equipment with a high degree of expertise are needed to pick up anomaly earlier. Some of the cord problems can also be tackled by identification of malpresentations early and availability of emergency obstetric care unless brought late in the hospital. Birth asphyxia is another cause

of neonatal death. Better use of partogram and timely intervention during delivery will decrease the incidence. Infections, multiple pregnancies, meconium aspiration syndrome, severe IUGR, obstructed labor, gestational, oligohydramnios, and severe anemia are other causes.

High stillbirth rates add to PMR for the country as seen in our case. A high percent of unregistered cases are associated with high stillbirth rate (total = 180; 119 unbooked cases). Of concern, antepartum deaths are more with 151 among which 104 were unbooked cases. Developing countries are particularly affected and continue to have high stillbirth rates compared with those of the developed world, where a decline has been observed over the last decades. It is estimated that stillbirth rates for developing countries are as high as 25.5/1000 deliveries, compared with 5.3/1000 deliveries for developed countries.<sup>18</sup>

Effective antenatal care is still lacking among the pregnant women. We still need to reduce more by not only awareness of proper antenatal checkup but the establishment of emergency obstetric care as well as essential newborn care. The number of stillbirths has reduced more slowly than has maternal mortality or mortality in children younger than 5 years, which were explicitly targeted in the Millennium Development Goals. The Every Newborn Action Plan has the target of 12 or fewer stillbirths per 1000 births in every country by 2030 which in turn will reduce the Under 5 Mortality Rate. Early diagnosis and control of hypertension, early detection of congenital anomaly, and prevention of maternal infections, proper intrapartum management, and an intensive neonatal unit will further decrease it. Fetal autopsy in future may detect many unknown causes. Socioeconomic status and literacy influences adverse pregnancy outcome, hence education automatically increases awareness and help in overall improvement.

## CONCLUSION

In the present study, the PMR was more in the unbooked cases. Stillbirths accounted for a major chunk of perinatal mortality. Adequate antenatal care can thus prevent many future consequences of low birthweight babies, stillbirths, and neonatal deaths. Early registration helps in proper evaluation and identification women at risk. Improving the Women's education not only improves effective ANC but also improves awareness especially during emergencies.

## RECOMMENDATIONS

First, community awareness and health education on the availability and importance of antenatal care services

should be scaled up. This may improve awareness of timing and adherence to prenatal services.

Second, an inquiry should be conducted on the supplementation intake among women who access antenatal services. In that way, possible causes may be identified and addressed.

Third, an exploration should be made of the possibility of introducing ultrasound screening at least once during pregnancy for all women attending antenatal care in the region. In that way, fetal well-being may be assessed, and possible supportive measures may be implemented.

Finally, pre-pregnancy health awareness and education should be enhanced. Women need to be educated about healthy living, alcohol avoidance, smoking, and pregnancy planning in terms of timing and spacing.

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# Evaluation of Hospital Supply and Locally Available Disinfectants by In-use Test in Bacteriology Laboratory of Tertiary Care Hospital

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## Abstract

**Introduction:** Hospital-acquired infection (HAI) is an infection that is contracted in the hospital environment or any other clinical settings where infection is spread to the susceptible patients from health-care staff, contaminated equipment, and environment. The use of disinfectants is important in preventing HAI. Rationalization of the use of disinfectants in hospitals is desirable for the purpose of proper quality control measurement. Because of potency loss on standing and presence of organic matter, disinfectants used in hospital laboratory must be tested periodically. Although the various methods of testing disinfectants have the same final purpose of measuring the antimicrobial activity, some of them help in selecting right dilution of disinfectants for use and other evaluate the efficacy of disinfectants which are already in use. For quality control in clinical bacteriology laboratory “in-use” test is recommended.

**Purpose:** The aim of this study was to analyze the efficacy and costs of the three disinfectant materials-conventional liquid hospital supplied phenol (1%), locally acquired phenol crystal (2 m%), conventional hypochlorite solution (1%), and pitting them against another conventional and standard disinfectant of 2% hospital supplied liquid phenol.

**Materials and Methods:** All the disinfectants at selected proposed dilutions were tested for bactericidal efficacy by “in-use” test. This test was used to detect the number of living organisms in a vessel of disinfectant solutions which were in actual use. It was performed on disinfectants in discard jars using a standard protocol.

**Results:** The study shows 1% conventional hypochlorite solution and 2% local phenol crystals are equally efficient bactericidal with that of the 2% conventional liquid phenol. Hypochlorite solution is most costly where phenol crystal is cheap and available locally.

**Conclusion:** Instead of expensive aldehyde containing commercially available agents, conventional liquid phenol, and locally available phenol crystal with their comparable low cost and similar efficacy can be used.

**Key words:** Bacteriology, Disinfectants, Hypochlorous acid, In-use test, Phenol, Quality control

## INTRODUCTION

Nosocomial infections, also called “hospital-acquired infections” (HAI), are infections acquired during hospital

care which are not present or incubating at admission. Infections occurring more than 48 h after admission are usually considered nosocomial. They are based on clinical and biological criteria and include approximately 50 potential infection sites such as urinary tract infections, surgical site infections, nosocomial pneumonia, nosocomial bacteremia, and others.<sup>1</sup> Nosocomial/hospital acquired/healthcare associated infection occurs worldwide at the rate of 5-10%.<sup>2</sup> The use of disinfectants is important in hospital infection control as failure can result in many such HAI leading to increased cost, mortality, morbidity.<sup>2</sup>

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Disinfectants can be used either as surface disinfectants or by immersing the contaminated objects in the solution.<sup>3</sup> The activity of disinfectants as germicides against microorganisms depends on intrinsic qualities of the organism like number and location of microorganisms, innate resistance of microorganisms along with external physical environmental and chemical factors such as temperature, contact period, pH, potency and concentration of disinfectant, bioburden, organic soil and hardness of water used for dilution, biofilm.<sup>3,4</sup> Efficiency and potency of disinfectants depend on each of these factors. There is least awareness among the healthcare providers about choosing an appropriate disinfectant, especially in small health care settings of developing countries. Usually, an agent with wide-range of antimicrobial activity is selected based on the literature provided by the manufacturers.<sup>3</sup>

While certain methods help in selecting right dilution of disinfectants for use, others test the efficacy of disinfectant already in use. For evaluation of their activity, various tests are available like minimum inhibitory concentration (which is the lowest concentration of the disinfectant that inhibits the growth of a known strain of bacteria), Rideal-Walker test,<sup>4</sup> Chick-Martin and Garrod tests (based on the phenol coefficient of disinfectants),<sup>5</sup> capacity-use-dilution test (Kelsey and Sykes, 1969),<sup>6</sup> modified by Kelsey and Maurer in-use test, 1974 (measure the efficacy of disinfectants already in use for a particular period and condition),<sup>7</sup> stability test and various other microbial time kill assay.<sup>6</sup> Some other tests such as suspension test (qualitative and quantitative), practical tests, and surface killing test are also to be mentioned.<sup>8</sup> As all these standard tests cannot be performed by the laboratories belonging to small hospitals, one has to be solely dependent on the literature provided by the manufacturer regarding the efficiency of the disinfectants which are usually broad-spectrum antimicrobial agent suitable for various applications.<sup>3</sup>

In view of the above, the following short study was planned with an aim to evaluate and to compare the practically achieved bactericidal efficacy and cost effectiveness of hospital supplied disinfectants with some locally available disinfectant product in the bacteriology laboratory of a tertiary care rural hospital. The efficacy was tested by performing Kelsey and Maurer's in-use test.

## MATERIALS AND METHODS

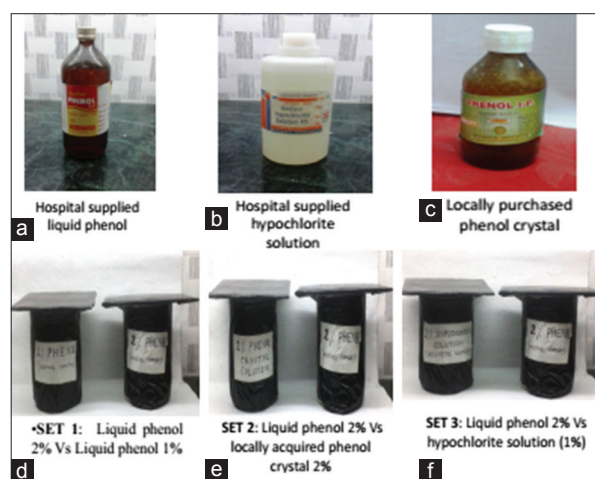
In the absence of any universally agreed test methods and to prevent malpractice by the manufacturers Kelsey and Maurer's "in-use" test was chosen to establish the efficacy of disinfectants at the in-use concentration against a significant bacterial challenge at an ambient temperature.<sup>9</sup>

This study was conducted at bacteriology laboratory of Bankura Sammilani Medical College Hospital, Bankura as a laboratory-based experimental study over 3 months. Effectiveness of two conventionally used hospital supplied disinfectants (phenol in two different concentrations and 1% hypochlorite solution) and one locally available disinfectant reagent were studied using this test.

The hospital supplied conventional disinfectants were phenol (80% W/V) manufactured by Indian Drug House (West Bengal, India) taken in two different concentrations of 1% and 2% and hypochlorite solution (4%) manufactured by Stanbio Reagent Pvt. Ltd. (Kolkata, India) used in a concentration of 1%. Locally purchased commercially available phenol/carbolic acid crystal manufactured by New Bengal Drug House (Kolkata, India) was used for comparison at a concentration of 2% (Figure 1).

For the biomedical wastes from bacteriology and tuberculosis laboratory, the recommended effective concentration of phenol for spillage or cleaning is 2%.<sup>9</sup> Phenol from hospital supply was used in this study in two concentrations, the recommended 2% and also 1% solution (as certain references have mentioned this to be bactericidal by leaking the amino acids from the bacterial cell).<sup>10</sup> Furthermore, 2% solution was made from locally acquired phenol crystals. Hospital supplied phenol was also taken in 1% concentration for comparison as it acts as bactericidal. Hospital supplied conventional 1% hypochlorite solution was also chosen as it is appropriate for spillage and where contaminants are present.<sup>9,18</sup>

Considering 2% liquid phenol from hospital supply as the gold standard, bactericidal efficacy and cost-effectiveness



**Figure 1:** (a) Hospital supplied liquid phenol. (b) Hospital supplied hypochlorite solution. (c) Locally purchased phenol crystal. (d) SET 1: Liquid phenol 2% versus liquid phenol 1%. (e) SET 2: Liquid phenol 2% versus locally acquired phenol crystal 2%. (f) SET 3: Liquid phenol 2% versus hypochlorite solution (1%)

of the other three solutions were tested and compared. These were hospital supplied liquid carbolic acid (1%) having market price of Rs. 130 of 500 ml (80% w/v), locally acquired phenol crystal (made up to 2 m%) with the cost of Rs. 30/100 g, hospital supplied hypochlorite solution (1%) having cost Rs. 95/500 ml of 4% solution (Table 1).

Hypochlorite solution decays rapidly and readily gets inactivated by organic material and light and also it is corrosive to metal at high concentration (more than 0.05%). Therefore, this test was performed with freshly prepared disinfectant using distilled water in dark glass jars each containing 500 ml of disinfectant solutions in the specific concentrations mentioned. These solutions were left overnight as recommended in these jars after dropping bacteriological contaminated materials in them throughout the working hours.<sup>10</sup> The next day, 1:10 dilution of the contents of the jars was made in nutrient broth so that the tested disinfectants became neutralised.<sup>9</sup> Each of the nutrient agar plates (product number M001., HiMedia Laboratories (P) Ltd. Mumbai, India) was marked at 10 different sites and with a “50-dropper” pipette, and 10 small drops each of 0.02 ml were then transferred in those 10 different areas of two well dried nutrient agar plates. For each set, one plate was then incubated at 37°C for 3 days while the other was held at room temperature for 7 days. The number of drops that yielded growth was counted after incubation. If growth was more than five drops on either plate, it represented failure of disinfectant.<sup>8,9</sup> Such a result was considered as approximately 1000 living organisms 1 ml in the tested sample of disinfectant.<sup>21</sup> In the study, each disinfectant solution was paired with the gold standard, that is 2% hospital supply phenol and each pair was tested daily in the bacteriology laboratory for 14 days. Therefore, three such pairs were tested over 6 weeks in the first cycle. The whole process was then repeated in the next 6 weeks. Hence, two such cycles of the study were completed in 3 months (Figure 1).

For performing the test, that is, to prepare 500 ml of each of the disinfectant solutions 28 times (14 times each for two cycles) it costed Rs. 532 for 1% hypochlorite solution (market price Rs. 95/500 ml of 4% hypochlorite solution), Rs. 91 and Rs. 45.5 for 2% and 1% conventional hospital supplied liquid phenol, respectively, as this liquid phenol had market price Rs. 130/500 ml of 80% (w/v) solution. The cost of

making 500 ml of 2% phenol from locally purchased phenol crystal was Rs. 84 (market price Rs. 30/100 g) (Table 1).

## RESULTS

Hospital supplied liquid phenol (2%) that is the gold standard in this study consistently showed growth not more than five colonies per plate for at least 12 days out of the 14 days cycle in all the tests. Hospital supplied liquid phenol (1%) showed satisfactory result that is growth of not more than five colonies per plate for 10 out of 14 days and nine out of 14 days in the consecutive two cycles, respectively. Hypochlorite solution (1%) showed growth of not more than five colonies per plate for 12 out of 14 days in both the cycles. Whereas, 2% solution made from locally available phenol crystal showed a satisfactory result of not more than five colonies per plate for 12 out of 14 days and 13 out of 14 days for the two cycles, respectively (Table 2 and Graph 1). The colonies on examination showed growth of *Klebsiella pneumoniae*, *Escherichia coli*, *Pseudomonas aeruginosa* (Figure 2). 2% liquid phenol which is recommended for use in tuberculosis and general bacteriological laboratory was chosen as the gold standard to validate this study.<sup>9</sup> In terms of efficacy, hypochlorite solution (1%) showed satisfactory result. Therefore, it can substitute the 2% hospital supplied liquid phenol. Efficacy of 2% locally available phenol crystal is comparable to the 2% liquid phenol. On the other hand, 1% liquid phenol shows comparatively less bactericidal effect than

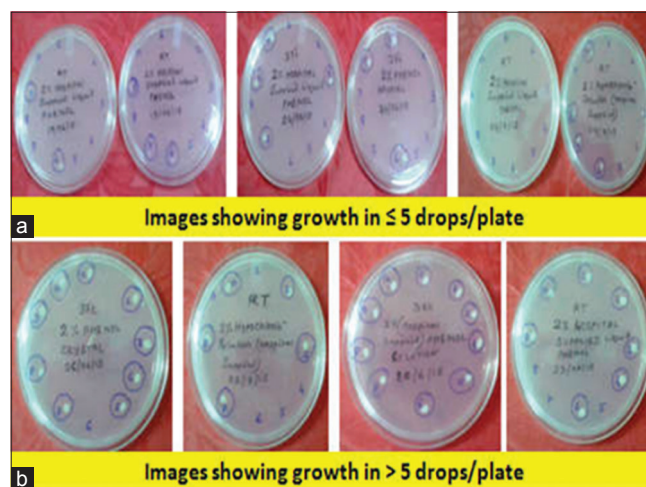
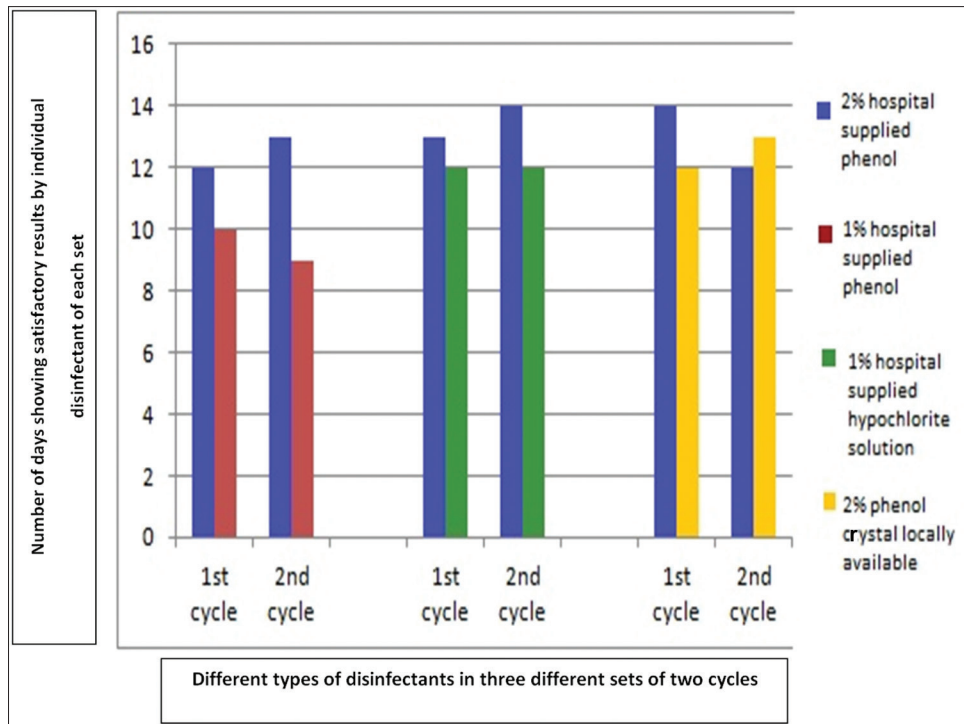


Figure 2: (a) Growth in ≤ 5 drops/plate. (b) Growth in > 5 drops/plate

Table 1: Cost of disinfectants

Disinfectants	Market price	Total costs to prepare 500 ml of such tested solution 28 times	Proportion (in terms of cost)
1% hypochlorite solution	Rs. 95/500 ml of 4% hypochlorite solution	Rs. 532	5.85
2% hospital supplied liquid phenol	Rs. 130/500 ml of 80% (w/v) solution	Rs. 91	1.0
1% hospital supplied liquid phenol	Rs. 130/500 ml of solution of 80% (w/v)	Rs. 45.5	0.5
2% locally purchased phenol crystal	Rs. 30/100 g	Rs. 84	0.92



**Graph 1: Overall comparative efficacy of three disinfectants in four different concentrations by in-use test method, considering 2% phenol liquid as the standard one**

**Table 2: Effectiveness of disinfectant**

Disinfectants	1 <sup>st</sup> cycle satisfactory result (days)	2 <sup>nd</sup> cycle satisfactory result (days)
In 1 <sup>st</sup> set		
Hospital supplied phenol (2%)	12	13
Hospital supplied phenol (1%)	10	9
In 2 <sup>nd</sup> set		
Hospital supplied phenol (2%)	13	14
Hospital supplied hypochlorite solution (1%)	12	12
In 3 <sup>rd</sup> set		
Hospital supplied phenol (2%)	14	12
Locally available phenol crystal (2%)	12	13

that of the standard 2% phenol Graph 1. As 1% phenol had poor bactericidal effect, it was considered to be unsuitable for the use in bacteriology and tuberculosis laboratory and cost effectiveness was not considered. 1% hypochlorite shows the same efficacy with that of the 2% liquid phenol both as higher cost whereas cost of 2% phenol made up from the locally available crystal is comparable or little less than the hospital supplied liquid phenol. In comparison to 2% hospital supplied liquid phenol (standard) and 1% hypochlorite proportion of cost is 5.85, whereas it is 0.92 with 2% phenol from locally purchased phenol crystal Table 1.

## DISCUSSION

Because of increasing resistance to antimicrobials and even disinfectants as evident in some recent international scientific research studies,<sup>11-15</sup> it is essential to perform efficacy testing of disinfectants in a regular manner in health care facilities. A study in Summerfield Hospital at Birmingham in 1972 showed satisfactory assessment of the contamination of disinfectants by the “in-use” test, along with membrane filtration technique.<sup>22</sup> Another study in Belgium reported the field test or the in-use test as one of the important tests for disinfectant.<sup>23</sup> Some earlier literature study revealed that there was no WHO recommended clear number of days before discarding disinfectants in the in-use method.<sup>24</sup> Some of the researchers showed antimicrobial activities of disinfectants were concentration dependent. They confirmed that if appropriate concentrations are not used even in the in-use testing, there will be contamination of disinfectants by various organisms like *P. aeruginosa*, *S. aureus*, and *Proteus* spp.<sup>22,25-27</sup> A recent study in Nigeria reported the degree of failure of a disinfectant is highest in constant use at beyond 2 weeks of the use. This finding clearly mentioned the need to periodically check the effectiveness of in-use disinfectant solutions for the purpose of early detection of the threat of disinfectant failure.<sup>24,28</sup> Our study results reveal that phenol must be used at a concentration of 2% otherwise its efficacy will be reduced. Alternatively, 1% hypochlorite solution can be used though it is not cost-

effective. Moreover, some of the previous studies highlighted its ineffectiveness against organic materials.<sup>19,20</sup> According to the logistic management, activity-based costing technique, which is a widely accepted and utilized method of production costing was used to calculate cost effectiveness. This balances two basic targets that are quality of service and low cost.<sup>18</sup> Our study result showed, 2% phenol, made from phenol crystal can be good alternative both in terms of efficacy and cost-effectiveness. Therefore, it can easily be used in remote health care setups where central supply may be erratic or those having limited resources. Proper biomedical waste disposal is an important aspect for control and prevention of HAI. As this in-use test shows reproducible result, it can be easily applied in the peripheral laboratory set ups for quality control purpose where other standard tests cannot be performed so easily.<sup>2</sup> Other germicides healthcare institutions should also be thoroughly evaluated for their efficacy and cost-effectiveness.<sup>16</sup>

Limitation of this study is that we tested only for the bactericidal effect of few disinfectants, but the considerable data generated from this type of study can be utilized for making hospital infection control policy.

## CONCLUSION

Although the utility of high-level disinfection and sterilization mandates effective clearing, no single real-time test exists to employ in a clinical setup to verify proper disinfectant.<sup>17</sup> Our study concludes that the most simple and acceptable method of in-use test can be performed in hospital laboratory for the biomedical wastes (category 3) to confirm the chosen disinfectant which has been effective under specific conditions along with its duration of use.

Along with the testing method, this short study also generated suitable data regarding bactericidal efficacy for the different type's disinfectants which can be utilized for hospital infection control policy. Therefore, in this era of expensive commercially available aldehyde containing disinfectants such as Des Net, Hi-giene, Clea-N-sept, Bacillocid special, and nonaldehyde containing newer hospital disinfectants such as Virkon, Novacide, Silvidice,<sup>3</sup> locally available phenol crystal (used domestically to avoid snake) with its least cost, availability and good bactericidal efficacy can replace others to equip discard jars especially in rural laboratory setup if hospital supplied phenol is not available.

Therefore, this study is relevant regarding the selection of the appropriate disinfectants in the bacteriology laboratories with their effective concentration and period of use, cost and availability. Along with this, the "in-use" technique is proved to be one of the simplest methods

of testing the disinfectants, which is already in use in bacteriology laboratory for the purpose of maintain good quality control in biomedical waste disposal.

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# Determinants of Abnormal Kidney Function Tests in Diabetes Patient Type 2 in Libya

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## Abstract

**Introduction:** Diabetes mellitus (DM) is among the most common non-communicable diseases. Humans around the world face many health threats. One of the most significant threats is DM, often simply referred to as diabetes. Although it has been centuries since DM was first recognized, it is still not fully understood and managed.

**Materials and Methods:** The target population was Type II diabetic males and females aged 40-60 years were selected at random among patients seeking medical care at the Hospital of El-Beida, Libya. The number of patients with Type II diabetic comprised 103 diabetic cases (79 males + 24 females). 39 healthy controls (29 males + 10 females), living under the same socio-economic conditions of the diabetic patients, were selected to serve as controls.

**Results:** Patients with diabetes 5 years were 60 (58.25%), whereas those with diabetic duration of 5-10 years were 27 (26.22%). The rest of patients 16 (15.53%) had diabetes for more than 10 years. The mean age of the patient was  $56.10 \pm 7.82$  years. Type 2 diabetes is a disease associated with abnormal carbohydrate metabolism, which arises due to insulin deficiency as insulin is the key hormone responsible for glucose homeostasis in blood.

**Conclusion:** In conclusion, in Libya diabetic patients, we concluded that biochemical parameters of kidney functions are associated with a worsening in insulin action and predicts the development of Type 2 diabetes.

**Key words:** Diabetes mellitus, Kidney function, Libya diabetic patients

## INTRODUCTION

Diabetes mellitus (DM) is among the most common non-communicable diseases. Humans around the world face many health threats. One of the most significant threats is DM, often simply referred to as diabetes. Although it has been centuries since DM was first recognized, it is still not fully understood and managed.<sup>1</sup> Diabetes now affects 7% of the world's adult population. Middle East occupies the second region after North America with the highest diabetes prevalence rates (9.3%), and this number is expected to double in <20 years.<sup>2</sup> However, the Libyan national non-communicable diseases survey in 2009 reported a prevalence of diabetes of 16.4%.<sup>3</sup> In

Libya population, the Type II diabetes affected >70% in Libya which is the highest prevalence in North Africa and among Arabic nations. The most possible cause is eating habit.<sup>4</sup> Kadiki *et al.*<sup>5</sup> reported that DM is as frequent in Libya as in other Mediterranean countries. Libya has the uncertain destination of being home to the huge number of people suffering from diabetes like in any other country. In diabetes, the cells do not receive glucose and most of it is accumulated in the blood. Too much sugar in the blood can lead to serious health problems, including heart disease and damage to the nerves and kidneys. Failing to control diabetes can give rise to many complications.<sup>6</sup> Diabetic kidney disease takes many years to develop. Overall, kidney damage rarely occurs in the first 10 years of diabetes, and usually, 15-25 years will pass before kidney failure occurs. The kidneys excrete metabolic waste products and regulate the serum concentration of a variety of substances. At some stage during the course of renal disease, the following routinely measured substances often become abnormal and the extent of the abnormality generally depends on the severity of the disease.<sup>7</sup> Serum creatinine and urea concentrations

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change inversely with changes in chronic renal failure (glomerular filtration rate [GFR]) and are, therefore, useful in gauging the degree of renal dysfunction.<sup>8</sup> Urea, uric acid, and creatinine are the parameters to diagnose functioning of the kidney. Changes in serum creatinine concentration more reliably reflect changes in GFR than do changes in serum urea concentrations. Creatinine is formed spontaneously at a constant rate from creatinine, and blood concentrations depend almost solely upon GFR. Urea formation is influenced by a number of factors such as liver function, protein intake, and rate of protein catabolism.<sup>8,9</sup> Biologically, uric acid plays an important role in worsening of insulin resistance in animal models by inhibiting the bioavailability of nitric oxide, which is essential for insulin-stimulated glucose uptake.<sup>10</sup> Consequently, this study aims to evaluate the kidney function among diabetes patients compared to non-diabetic control group.

## MATERIALS AND METHODS

The target population was Type II diabetic males and females aged 40-60 years were selected at random among patients seeking medical care at the Hospital of El-Beida, Libya. The number of patients with Type II diabetic comprised 103 diabetic cases (79 males + 24 females). 39 healthy controls (29 males + 10 females), living under the same socioeconomic conditions of the diabetic patients, were selected to serve as controls. They had no symptoms of diabetes and had fasting serum glucose levels <120 mg/dl. There was no evidence of any acute illness. The age distribution of the healthy controls was approximately similar to that of the patients. A meeting interview was used for filling in the questionnaire, which designated for matching the study need. All interviews were conducted face to face by the researcher himself. During the study, the interviewer explained to the participants any of the confused questions that will not clear to them. Most questions were the yes/no questions, which offer a dichotomous choice.

All participants were anonymized by numbering them and numbering the blood samples taken from them. All participants were asked to fast overnight for a period of about 8 h (12 pm - 8 am), during which no treatment (insulin or hypoglycemic drugs) was allowed to be taken. The patients were also given a questionnaire to fill in which contained several questions regarding their lifestyle habits and medical history for epidemiological study. Blood samples were collected from 103 Type II diabetic patients and 39 controls. Fasting overnight venous blood samples (about 7 ml) were drawn by the researcher himself into Vacutainer plane tubes from all individuals. The blood was left for a while without anticoagulant to allow blood to clot.

Then, serum samples were obtained by centrifugation at room temperature at 4000 rpm/10 min.

Blood samples were obtained at recruitment (non-fasting) and measured at routine hospital laboratories using an automated biochemistry analyzer. Serum glucose concentration was measured by the method of Trinder,<sup>11</sup> and serum urea and creatinine were determined by methods of Patton and Crouch<sup>12</sup> and Henry *et al.*,<sup>13</sup> respectively. Serum uric acid was determined according to the method of Kayamori *et al.*<sup>14</sup>

All the data from despotic diabetic patients and age-matched controls from different experiments were analyzed and compared using Student's *t*-test. The results were expressed as mean  $\pm$  standard deviation. The significant test was applied at  $P < 0.05$ .

The percentage difference was calculated according to the formula:

Percentage difference = (mean of patient-mean of control)/(mean of patient + mean of control/2)  $\times$  100. Range of minimum and maximum values was used.

## RESULTS AND DISCUSSION

### Distribution of the Study Population

Table 1 illustrates general characteristics of the study population. 142 participants were recruited to the study consisting of 103 patients with diabetes (cases) and 39 participants without diabetes (controls). The average age was  $56.10 \pm 7.82$  years, ranging between 42 and 67 years in diabetic patients and  $54.97 \pm 6.34$  years in a range of 39 through 61 in the control group. Among the patient's group, 79 patients were males representing 76.7% and 24 patients were females representing 23.3%, on the other hand, 29 of the control group were male (74.4%) and 10 were female (25.6%). The number of patients from each area was selected because the number of diabetic patient in El-Beida was not available.

Table 2 summarizes the distribution of diabetic patients by diabetes duration. Patients with diabetes 5 years were 60 (58.25%), whereas those with diabetic duration

**Table 1: Participants recruited for this study**

Characteristics	Healthy control	Diabetic
Number of Participants	39	103
Age group range (min-max)	54.97 $\pm$ 6.34 (39-61)	56.10 $\pm$ 7.82 (42-67)
Gender	29 males and 10 females	79 males and 24 females
Diabetic status	Non-diabetic	T2DM

of 5-10 years were 27 (26.22%). The rest of patients 16 (15.53%) had diabetes for more than 10 years. The mean age of the patient was  $56.10 \pm 7.82$  years. It was reported that Type II DM usually develops after age 40 years.<sup>15</sup> The results that more than half of patients had diabetes since <5 years do confirm the idea that Type II diabetes has long asymptomatic pre-clinical phase, which frequently goes undetected. At the time of diagnosis, the patient could have one or more diabetes complications.<sup>16</sup> In the current study, the finding was not found any associated with complications (liver disease, cardiovascular disease, kidney disease, and recurrent infection) in relation to duration of diabetes. These findings are confirmed by self-report questionnaire. However, this point still needs further investigation. The prevalence of such symptoms was positively associated with the progress of the disease, i.e., the longer the duration of DM. Several studies reported similar diabetic complications with increasing rates upon disease progress.<sup>17,18</sup>

### Serum Glucose of Diabetic Patients

Type 2 diabetes is a disease associated with abnormal carbohydrate metabolism, which arises due to insulin deficiency as insulin is the key hormone responsible for glucose homeostasis in blood (Kumar *et al.*, 2005). As shown in Table 3, it was found that there was a significant ( $P < 0.05$ ) increase in the mean serum glucose level in patients than that in controls ( $98.48 \pm 8.97$  vs.  $210.0 \pm 48.65$  mg/dl, % difference = 84.20).

**Table 2: Distribution of diabetic patients (n=103) by diabetes duration**

Duration of diabetes (year)	Number (%)
<5	60 (58.25)
5-10	27 (26.22)
>10	16 (15.53)

**Table 3: The results of serum glucose of diabetic patients and controls**

Parameter	Healthy control (n=39)	Diabetic (n=103)	Percentage difference
Glucose (mg/dl)	$98.48 \pm 8.97$	$210.0 \pm 48.65^*$	84.20
Range (min-max)	79-121	148-387	

\* $P < 0.05$  for diabetic compared to control group. All results are expressed as mean  $\pm$  SD. SD: Standard deviation

**Table 4: The results of the kidney function parameters measured in serum of healthy controls and diabetic patients**

Parameters	Healthy control (n=39)	Diabetic (n=103)	Percentage difference
Urea (mg/dl) range (min-max)	$28.74 \pm 2.13$ (18.0-34.0)	$47.24 \pm 12.48$ (37.0-57.0)*	48.70
Creatinine (mg/dl) range (min-max)	$0.79 \pm 0.04$ (0.69-0.97)	$1.19 \pm 0.39$ (0.96-1.34)*	40.40
Uric acid (mg/dl) range (min-max)	$4.98 \pm 0.81$ (3.89-6.02)	$8.19 \pm 2.42$ (6.48-8.97)*	48.80

\* $P < 0.05$  for diabetic compared to control group. All results are expressed as mean  $\pm$  SD. SD: Standard deviation

Diabetic patients are characterized by abnormalities in glucose metabolism in several organs, skeletal muscle glucose disposal is reduced, hepatic glucose production is increased, and insulin-independent glucose uptake into the lens and neural tissue are increased.<sup>19</sup> Although the actual mechanisms of insulin resistance in Type 2 diabetes remain unknown, several steps in the uptake and intracellular handling of glucose are probably affected.<sup>20</sup> Measuring blood glucose is one-way of monitoring diabetes. In this study, diabetic patients have an abnormal level in blood glucose compared with non-diabetics. High levels of blood glucose of diabetic patients due to lack of or resistance to insulin, same results were found by Abdelgadir<sup>21</sup> and Bergenstal *et al.*<sup>22</sup> In their studies of diabetic population, in which they conclude that the fasting blood glucose level is also elevated, and this indicates poor control of DM. In fact, DM is characterized by hyperglycemia together with biochemical alterations of glucose.<sup>22</sup>

### Serum Urea, Uric Acid, and Creatinine of Diabetic Patients

Impairment in renal function is assessed by estimating the serum urea levels and the serum creatinine levels.<sup>7</sup> Impairment of renal function due to Type 2 diabetic mellitus was assessed by measurement of serum concentrations of urea and creatinine in diabetic patients and healthy controls. Data listed in Table 4 showed that the mean serum urea concentrations were significantly ( $P < 0.05$ ) decreased in diabetic patients compared to controls ( $28.74 \pm 2.13$  vs.  $47.24 \pm 12.48$  mg/dl, % difference = 48.70). Similar trend was found for creatinine and uric acid concentration ( $0.79 \pm 0.04$  vs.  $1.19 \pm 0.39$  mg/dl, % difference = 40.40,  $4.98 \pm 0.81$  vs.  $8.19 \pm 2.42$  mg/dl, % difference = 48.80, respectively). This change was also significant ( $P < 0.05$ ). Urea is formed by the liver as an end product of protein breakdown and is one marker of the kidney function.<sup>23</sup> An increase in serum urea observed here might be due to impairment in its synthesis as a result of impaired hepatic function and/or due to disturbance in protein metabolism.<sup>23,24</sup>

Creatinine is a waste product that is normally filtered from the blood and excreted with the urine. Higher creatinine levels in diabetic patients may be related to disturbance of kidney function.<sup>23</sup> In addition, the observed increases in urea and creatinine may be explained on the basis of glomerular hyper-filtration due to increase creatinine clearing from blood.<sup>25</sup>

Serum creatinine and urea are established markers of GFR. Although serum creatinine is a more sensitive index kidney function compared urea level. This is because creatinine fulfills most of the requirements for a perfect filtration marker.<sup>23,26</sup> The present results support by several studies, it has been reported that there is a clear association of serum urea with fasting blood sugar.<sup>1,27,28</sup> Manjunatha *et al.*<sup>23</sup> concluded in their study that blood urea and creatinine is accepted to assess the renal function.

As DM is the major cause of renal morbidity and mortality, so a good control over the sugar level can halt the progression of renal damage. Biologically, uric acid plays an important role in worsening of insulin resistance in animal models by inhibiting the bioavailability of nitric oxide, which is essential for insulin-stimulated glucose uptake.<sup>10</sup> Reports by Adler *et al.*<sup>29</sup> showed that raised plasma creatinine and urea levels in diabetic patient indicated a pre-renal problem such as volume depletion. Investigations by Judykay<sup>30</sup> suggested that high creatinine levels noted in diabetic patients might be due to impaired function of the nephrons. Increased serum creatinine and blood urea levels recorded in Type 1 and Type 2 DM patients could be attributed to a fall in the filtering capacity of the kidney thus leading to accumulation of waste products within the system. Although serum creatinine and blood urea tests can expose the patient's renal function, serum creatinine is a more sensitive indicator, as many extrarenal conditions such as dehydration, can increase urea levels. However, serum creatinine levels alter very little except in renal dysfunction.<sup>31</sup>

Serum uric acid is positively associated with serum glucose in healthy controls;<sup>32</sup> it is not clear whether raised serum uric acid predicts the risk of Type 2 diabetes.<sup>33,34</sup> This present study is investigated the association between serum uric acid and risk of diabetes in the El-Beida city. Table 4 presents the association between increasing serum uric acid levels and DM by hypertension status (48.80%). These results agree with previous studies, which reported that there is a positive association between high serum uric acid levels and diabetes,<sup>35-37</sup> whereas other studies reported no association [34] or an inverse relationship.<sup>38,39</sup>

Hence, it is recommended that these tests should be performed when patients are diagnosed as diabetics and at the time of follow-up, annually. A good control of blood glucose level is absolute requirement to prevent progressive renal impairment.

## CONCLUSION

In conclusion, in Libya diabetic patients, we concluded that biochemical parameters of kidney functions are associated

with a worsening in insulin action and predicts the development of Type 2 diabetes. These results support the hypothesis that the kidney is important in the pathogenesis of Type 2 diabetes, and that kidney parameter may be useful additional markers of patients at high risk for development of diabetes. Further studies on the kidney functions on diabetic patients need to be performed.

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# A Clinical Study and Management of Gastric Outlet Obstruction in Adults

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## Abstract

**Introduction:** Gastric outlet obstruction implies complete or incomplete obstruction of the distal stomach, pylorus, or proximal duodenum<sup>1</sup>. This may occur as an obstruction mass lesion, external compression or as a result of obstruction from acute enema, chronic scarring, and fibrosis or a combination of both.

**Aims and Objectives:** To determine the relative incidence of benign and malignant gastric outlet obstruction. To study the modes of presentation of gastric outlet obstruction. To study the outcome of management of gastric outlet obstruction.

**Materials and Methods:** The patients for this study have been selected from Mahatma Gandhi Memorial Hospital attached to Kakatiya Medical College Warangal from March 2013 to September 2014. In total, 50 in-patients of gastric outlet obstruction have been studied attached to Kakatiya Medical College, Warangal from March 2013 to September 2014. In total, 50 in-patients of gastric outlet obstruction have been studied.

**Observations and Results:** Of the 50 cases of gastric outlet obstruction, 26 had carcinoma antrum, 23 had cicatrized duodenal ulcer, and 1 had gastric outlet obstruction secondary to corrosive ingestion.

**Discussion:** The discussion is mainly in analysis and observation made regarding the presenting symptoms, signs, investigations, operative findings, management, and post-operative events in 50 cases of gastric outlet obstruction.

**Key words:** Gastrectomy, Gastric outlet obstruction, Gastrojejunostomy, Upper gastrointestinal endoscopy, Vagotomy

## INTRODUCTION

Gastric outlet obstruction implies complete or incomplete obstruction of the distal stomach, pylorus, or proximal duodenum.<sup>1</sup> This may occur as an obstruction mass lesion, external compression or as a result of obstruction from acute enema, chronic scarring, and fibrosis or a combination of both.<sup>1,2</sup>

Gastric outlet obstruction was described by Sir, James Walton as “The stomach you can hear, the stomach you can feel and the stomach you can see.”

Gastric outlet obstruction is not a single entity and it is the clinical and pathophysiological consequence of any disease process that produces a mechanical impediment to gastric emptying.<sup>3</sup>

Gastric outlet obstruction may be caused by a heterogeneous group of diseases that include both benign and malignant conditions.<sup>1,4</sup> In adults, mechanical obstruction due to ulcers, tumors, big polyps is common causes of gastric outlet obstruction.<sup>5</sup>

Until introduction of effective ulcer therapy, duodenal ulcer was the most common cause of gastric outlet obstruction and malignancy was attributed to only 0% of the cases. However, now in the era of H2 blockers and proton pump inhibitors, incidence of duodenal ulcer has been decreasing as symptomatic ulcer begin to respond to medical treatment, although this has not reflected to changes of complication like bleeding and perforation.<sup>6,7</sup>

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At the same time, the incidence of antral carcinoma of stomach producing gastric outlet obstruction has comparatively increased, which may be due to increased early diagnosis of the condition with the help of flexible fiber optic endoscope.

This study has been taken up to review the changes in the presentation of gastric outlet obstruction in view of changing trends in the management because of new drugs and investigatory modalities. The lack of uniformity in criteria in accepting a case of gastric outlet obstruction lead to differences in incidences and clinical features in different centers, still, any one of the followings can be used to diagnose gastric outlet obstruction. Projective vomiting of undigested food consumed previous day. Palpable hypertrophied stomach. Visible gastric peristalsis (VGP). Gastric succession of stomach on barium meal studies. A gastric residue of more than 500 ml in an adult. An aspirate of more than 40 ml on saline load test. Demonstration at operation of grossly narrowed gastric outlet.

In managing gastric outlet obstruction, measures employed are designed to improve the local condition of stomach, correct fluid and electrolyte imbalance, correct anemia, hypoproteinemia and vitamin deficiency, treatment of etiological conditions.

## MATERIALS AND METHODS

The patients for this study have been selected from Mahatma Gandhi Memorial Hospital attached to Kakatiya Medical College Warangal from March 2013 to September 2014. In total, 50 in-patients of gastric outlet obstruction have been studied. Inclusion criteria: Patients presenting with gastric outlet obstruction who are treated on in-patients basis. Patients willing for investigations and treatment. Exclusion criteria: Patients aged 20 years and below. Pregnant females, patient with a recent history of any abdominal surgeries. An elaborate study of these cases with regard to the history, clinical features, routine and special investigations, pre-operative treatment, operative findings, post-operative management, and complications in post-operative period is done.

In history, details were noted about presenting complaints, duration, history of acid peptic disease, features of metabolic disturbances, occupation and personal history including diet, bowel and bladder habits, smoking, and alcoholism. Through analysis of the findings of physical examination done, which included hydration status, VGP, mass, succession splash, hepatomegaly, and ascites. Associated conditions such as anemia, hypertension, and

diabetes were managed before surgery with physician's advice wherever required.

Hemoglobin level, bleeding time, clotting time, routine urine examination, chest screening, electrocardiogram, blood grouping, fasting blood sugar (FBS) and postprandial blood sugar, blood urea, serum creatinine, serum electrolytes were estimated as a part of general workup for surgery. Special investigations such as barium meal, upper gastrointestinal (GI) endoscopy, and ultrasonography (USG) abdomen were done wherever feasible.

Any one of the following criteria can be used to diagnose gastric outlet obstruction. Projective vomiting of undigested food consumed previous day, palpable hypertrophied stomach, VGP, gastric succession splash 3-4 h after the last meal, delayed emptying of stomach on barium meal studies, demonstration at operation of grossly narrowed gastric outlet.

### Management of Cases

Pre-operative treatment included correction of dehydration, metabolic status, anemia, intravenous (IV) H<sub>2</sub> blockers; liquid diet, and antacids were given along with twice a day stomach was for a minimum 3 days. According to the investigation reports and operative findings, definitive surgery was undertaken.

### Surgery Performed

Truncal vagotomy with gastrojejunostomy, Billroth II gastrectomy, Billroth II gastrectomy with feeding jejunostomy, posterior gastrojejunostomy, total gastrectomy with Roux-en-Y anastomosis, anterior gastrojejunostomy alone, anterior gastrojejunostomy with limbal anastomosis, and jejunostomy.

### Anesthesia

For all cases, general anesthesia was given.

### Post-operative Management

The patients were managed by Ryle's tube aspiration and intravenous fluids till the bowel sounds appeared. Oral feeding with fluids was then commenced, solids being given later. Early ambulation was encouraged, especially in elderly patients. Routine antibiotic was given during the immediate post-operative period. Regular monitoring of the temperature, pulse, respiratory rate, and blood pressure was done.

## OBSERVATIONS AND RESULTS

Of the 50 cases of gastric outlet obstruction, 26 had carcinoma antrum, 23 had cicatrized duodenal ulcer, and

1 had gastric outlet obstruction secondary to corrosive ingestion.

Causes	Number of cases (%)
Carcinoma antrum	26 (52)
Cicatrizated duodenal ulcer	23 (46)
Corrosive ingestion	01 (02)
Total	50 (100)

### Personal History in Present Series

1. Socioeconomic status: Majority of the patients were from low socioeconomic status
2. Diet: 90% of patients were taking mixed diet and 10% patients were taking vegetarian diet. 39 patients (78%) had history of irregular diet habits
3. Smoking: 68% of the patients were smokers in this series and 32% were non-smokers
4. Alcohol: 66% of the patients in this series gave history of consuming alcohol.

### Investigations

The following investigations were carried out before subjecting the patient for surgery. hemoglobin percent, FBS, blood grouping, serum electrolytes, urine routine, chest X-ray, ECG, barium meal examination, endoscopy, and USG examination done whenever possible. hemoglobin percent in majority (70%) of patients was 11 g%.

### Barium Meal Examination

Done in 14 cases, in 8 cases filling defect in the antrum was present. Dilated stomach with delayed emptying and deformed cap was present in 6 cases.

### Upper GI Endoscopy

Done in all cases, 26 cases of pyloric carcinoma diagnosed and confirmed with biopsy. 23 had cicatrized duodenal ulcer.

### Ultrasonographic Examination

Done in 32 cases, carcinoma pyloric region with ascitis was present in four cases. Ascitis with liver secondaries was present in 1 case. The rest showed normal study.

### Serum Electrolytes

In the present series, all patients were subjected to serum electrolyte estimation, out of them 9 patients showed electrolyte imbalance. All patients underwent pre-operative treatment to get the optimum metabolic status. The pre-operative treatment included liquid antacid and IV ranitidine. Stomach as using number 16 Ryle's tube with normal saline was given twice a day for 3 days before surgery.

All the patients were kept nil orally and on Ryle's tube aspiration for during varying from 3 to 10 days. Oral

sips were allowed after removal of Ryle's tube. IV fluids were stopped on the 5<sup>th</sup> to 10<sup>th</sup> post-operative day and patients started in semisolid diet. The patients were put on broad spectrum antibiotics, IV H2 receptor blockers, and analgesics.

### Post-operative Complication

Wound infection developed in two patients who were treated by repeated dressing and appropriate antibiotics. In four patients respiratory tract infection developed which was treated by chest physiotherapy and review of antibiotics. 5 patients of antral carcinoma were treated postoperatively by chemotherapy with 5-fluoro uracil. 18 patients of antral carcinoma were referred to MNJ Cancer Institute, Hyderabad, for further management. One patient of carcinoma pyloric region died on the 9<sup>th</sup> post-operative day. Rest of the patients had an uneventful post-operative period. Post-operative hospitalization ranged from 7 to 40 days with an average of 11 days.

## DISCUSSION

The discussion is mainly in analysis and observation made regarding the presenting symptoms, signs, investigations, operative findings, management, and post-operative events in 50 cases of gastric outlet obstruction admitted to Mahatma Gandhi Memorial Hospital Warangal during March 2013 to September 2014. Out of 50 cases:

- Gastric outlet obstruction secondary to carcinoma pyloric region - 26
- Gastric outlet obstruction secondary to cicatrized duodenal ulcer - 23
- Gastric outlet obstruction secondary to corrosive ingestion - 1.

The most common cause of gastric outlet obstruction is carcinoma of the pyloric antrum. The next most common cause is cicatrized duodenal ulcer. These observations reveal that the incidence of gastric outlet obstruction secondary to chronic duodenal ulcer as come down while that of malignancy has relatively increased. In this study, the most patients were in the sixth and seventh decade. In chronic duodenal ulcer cases, the maximum incidence seen in the age group of 31-40 years. The average age being 47.52 years with span from 22 to 73 years. Men outnumbered women by 10:5:1. In the series of Fisher *et al.*, the average age was 54 with span from 20 to 89 years and men outnumbered women by 2:1.

In antral carcinoma case, the maximum incidence is seen in the age group of 61-70 years. The youngest age of presentation is 32 years and oldest is 84 years with average being 59.73 years. Men outnumbered women by 5:25:1 as

compared to 5:5:1 observed by Yogiram and Chowdary. This higher incidence in males worldwide can be explained as because of more consumption of gastric irritants by males compared to females. 52% of the patients were manual laborers who gave a history of irregular diet habits, which seemed to contribute to disease process. The series of Donald D. Kozoll and Karl A. Meyer also showed the same pattern with the non-skilled day laborer group listed most frequently with obstruction.

In this series, 68% of patients had history of smoking and 66% had history of alcohol intake. Donald D. Kozoll and Karl A. Meyer reported this to be 7602 and 523%, respectively. These points to the commonly observed fact that a higher incidence of the use of alcohol and tobacco is seen in these patients and are significant risk factors.

Postprandial vomiting and epigastric pain are the main symptoms (96%) in this series. Vomiting is usually spontaneous and projectile type containing partially digested food particles. Other symptoms included anorexia (84%), weight loss (72%), postprandial epigastric fullness (68%), hematemesis (24%), malena (64%), and constipation (48%). In the series of Micheal L. Schwartz *et al.*, postprandial vomiting was the most common symptom (91%). Other symptoms included epigastric pain (86%) and weight loss (52%).

In the series of yogiram and chowdary epigastric pain was the most common symptom (87%). Other symptoms included postprandial vomiting (80%) and constitution (30%) Keith A. Kelly in his series reported intractable vomiting and weight loss in 54% of patients and upper gastrointestinal hemorrhage in 34%. Weight loss was seen in 59.5% of patients in the series of Donald D. Kozoll and Karl A. Meyer and 32% in the series of Harvey J. Dworken and Harold P. Roth. Thus, weight loss seemed to be significant in patients with pyloric obstruction and this point to the long-standing nature of the disease and the need for proper pre-operative nutritional supplementation in these patients.

In carcinoma pyloric antrum cases, pain (96.15%) was the leading symptom. Other symptoms included vomiting (92.30%), anorexia (84.62%), weight loss (65.4%), and postprandial fullness (57.70%). Hematemesis was present in 26.92%, malena in 69.23% and constipation in 50%.

Pain, vomiting, anorexia, and postprandial fullness (100%) were the leading symptoms in gastric outlet obstruction due to other causes. Pallor was present in 56% and dehydration was present in 22%.

VGP was seen in 69.56% of cicatrized duodenal ulcer cases. In the series of Yogiram and Chowdhary VGP was present in 74%.

Succession splash was seen in 65.22% of cicatrized duodenal ulcer cases while Harold Ellis observed succession splash in 64% of his cases.

VGP (38.46%) and succession splash (50%) were less prominent in malignant cases. This corresponds in observation made by Harold Ellis Palpable mass was present in 34.62% of malignant cases.

Blood group "O" was common in cicatrized duodenal ulcer patients (52.18%) followed by blood Group "A" (26.08%). This is significant as persons of blood Group "O" are about three times more likely to develop acid peptic disease than persons of other blood groups. Blood group "A" was common in malignant cases (50%). In the present series, 100% of cicatrized duodenal ulcer patients underwent truncal vagotomy with gastrojejunostomy.

In carcinoma antrum cases, 26.92% of the patients underwent Billroth II Polya gastrectomy and 42.30% patients underwent anterior gastrojejunostomy. 2 cases (7.70%) underwent Roux-en-Y anastomosis after total gastrectomy while 3 cases (11.54%) underwent anterior gastrojejunostomy with limb anastomosis. The remaining 3 cases underwent Billroth II gastrectomy with feeding jejunostomy. All the patients were subjected to a standard pre-operative treatment, which included stomach wash twice a day for 3 days before surgery. Preoperatively stomach was dilated in the majority of the cases. Postoperatively aspiration was continued till bowel movements established by noting bowel sounds, passing of flatus and gross reduction in quantity of Ryle's tube aspiration. Later on, patients were allowed to take oral fluids and then liquid and solid diet.

In this series, two patients had wound infection and were treated by repeated dressing and appropriate antibiotics. Four patients had respiratory tract infection and were treated by review of antibiotics and chest physiotherapy.

One patient of carcinoma pyloric region died on the 9<sup>th</sup> post-operative day.

The overall mortality rate was 2% (3.85% for malignant cases). Mortality rate was zero in case of stenosing duodenal ulcer.

Most of the stenosing duodenal ulcer cases were lost for follow-up. There has been no recurrence of symptoms in any of the cases that turned up for follow-up.

## CONCLUSION

Since the study has been based on a small number of cases, with a limited follow-up, it is rather difficult to come to

definite conclusions. However, some of the conclusions which can be drawn from this series are as follows:

1. The most common causes of gastric outlet obstruction in adults are carcinoma stomach with antral growth producing gastric outlet obstruction (52%) and cicatrized duodenal ulcer (46%)
2. In the vast majority of cases, the diagnosis can be established clinically
3. Upper gastrointestinal endoscopy should be mandatory in all suspected case of gastric outlet obstruction. It can diagnose the cause of obstruction very effectively than any other investigative modality
4. Number of cases with cicatrized duodenal ulcer as the chief etiological factor for gastric outlet obstruction is diminishing, and the number of cases of antral carcinoma of stomach as the cause of gastric outlet obstruction is increasing
5. Effective treatment in carcinoma stomach depends on early diagnosis.

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# Screening of High-Risk Women for Human Papillomavirus DNA with Qualitative Polymerase Chain Reaction and its Correlation with Liquid Pap Smear Cytology in a Semi-Urban Population

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## Abstract

**Introduction:** Cervical cancer is the second most common cancer in women. Human papillomavirus (HPV) is proved by various studies as the common etiologic agent for cervical cancer. So by diagnosing infection with HPV, prevention of developing an invasive cervical cancer is possible.

**Aim:** To study cervical cancer, screening/secondary prevention is to prevent invasive cervical cancer from developing by detecting and treating women with cervical intraepithelial neoplasia 2/3 lesions.

**Materials and Methods:** Using reflex panel liquid-based cytology, Pap smear and qualitative HPV L-1 gene was done gel-based polymerase chain reaction (PCR) method for all women in the age group of 25-65 years who attended our OPD with symptoms of leukorrhea.

**Results:** Qualitative PCR of the vaginal smear samples for HPV DNA testing does not correlate with liquid Pap smear cytology in clinically symptomatic patients with chronic cervicitis.

**Conclusion:** Cervical cancer screening through HPV DNA qualitative testing by PCR method in women is not reliable and real-time PCR testing to stratify the high-risk types of HPV may be a more accurate method.

**Key words:** Cervical cancer, Human papillomavirus, Liquid base Pap smear cytology

## INTRODUCTION

Cancer of the cervix is the most common gynecological malignancy worldwide.<sup>1</sup> More than 85% of the global burden occurs in developing countries, where it accounts for 13% of all female cancers. Furthermore, the mortality due to cervical cancer is higher in the developing countries where screening and treatment modalities are not commonly available or accessible compared with

the developed countries.<sup>2</sup> Every year in India, 122,844 women are diagnosed with cervical cancer and 67,477 dies from the disease. India has a population of 432.2 million women aged 15 years and older who are at risk of developing cervical cancer. It is ranked second most common cancer in women aged 15-44 years. India also has the highest age standardized incidence of cervical cancer in South Asia at 22, compared to 19.2 in Bangladesh, 13 in Sri Lanka, and 2.8 in Iran.<sup>3</sup> Hence, cervical cancer screening should begin at age 21 years. Pap cytology screening is recommended every 3 years for women between the ages of 21 years and 29 years. For women aged 30-65 years, co-testing with cervical cytology screening and HPV testing is preferred and should be performed every 5 years. Cervical carcinoma has its origins at the squamous-columnar junction and it can involve the outer squamous cells, the inner glandular

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cells, or both. A precursor lesion is dysplasia: Cervical intraepithelial neoplasia (CIN) or adenocarcinoma *in situ*, which can, subsequently, become invasive cancer. This process of tumorigenesis is slow. Longitudinal studies have shown that in 30-70% of patients with untreated *in situ* cervical cancer and will develop invasive carcinoma over a period of 10-12 years.<sup>4</sup> However, in about 10% of patients, precancerous lesions can progress from *in situ* to invasive in a period of <1 year. As it becomes invasive, the tumor breaks through the basement membrane invading the cervical stroma. Extension of the tumor in the cervix may ultimately present as ulceration, exophytic tumor, or extensive infiltration of underlying tissue, including the bladder or rectum. Human papillomavirus (HPV) has been found to be a necessary but not sufficient cause of cervical cancer. Of the more than 100 HPV types, 18 subtypes have been categorized as high-risk types, while the rest are low-risk types for cervical cancer. HPV prevalence among cervical cancer patients in India has varied from 87.8% to 96.67%.<sup>5-7</sup> Molecular studies have shown that HPV-16 and 18 are the two most common highly oncogenic types found in invasive cervical cancer, and out of these two, HPV-16 has been found more commonly.<sup>8</sup> The prevalence of other high-risk types is very low. Hospital-based studies showed a prevalence ranging from 9.9% to 16.6% among women with benign cervical cytology.<sup>9,10</sup> The critical components of a screening program are an acceptable good-quality screening test, prompt diagnostic investigations, appropriate treatment, and post-treatment follow-up. There is a strong evidence from non-experimental studies in developed countries such as Denmark and Finland that the incidence and mortality of cervical cancer can be reduced by screening.<sup>11</sup>

### Aim

To study cervical cancer screening/secondary prevention is to prevent invasive cervical cancer from developing by detecting and treating women with CIN2/3 lesions.

## MATERIALS AND METHODS

Location of the study conducted: Cancer OP, Thoothukudi Government Medical College, Thoothukudi.

Using reflex panel liquid-based cytology, Pap smear and qualitative HPV L-1 gene was done gel-based polymerase chain reaction (PCR) method for all women in the age group of 25-65 years who attended our OPD with symptoms of leukorrhea. The interpretation was done by the presence or absence of 158 base pair product of HPV DNA. The sensitivity and specificity of HPV testing were compared with routine cytology, both overall and for various age groups.

## RESULTS

Around 46% (10/22) of the screened population was in the 41-50 age groups. This age group confirms to that of the active sexual life and reproductive age (Table 1).

Abnormal findings were seen on clinical examination in 55% (12/22) of the screened population. The findings noted were hypertrophy of cervix (1/22), erosions in anterior, posterior, or both the cervical lips (9/22) (Figure 1).

Liquid Pap smear cytology was done using the reflex panel. It showed evidence of dysplasia in 83% of the screened population. Mild dysplasia was seen in 4% and moderate dysplasia was seen in 13% (Figure 2).

Qualitative HPV L - 1 gene analysis done by gel-based PCR method was negative in all the 22 persons (100%) screened (Figure 3). Screened population with positive clinical findings when compared with the results of liquid Pap smear cytology. Leukocyte particle concentration was positive in only 2/7 persons who had positive clinical findings but was negative in all the 15 persons with negative clinical findings,  $P = 0.091$  (Table 2).

Qualitative HPV L - 1 gene PCR was negative in all the persons with both positive and negative clinical findings,  $P = 1.000$  (Table 3).

**Table 1: Distribution of study patients**

Age group	Patients (%)
20-30	4 (18)
31-40	10 (46)
41-50	4 (18)
51-60	4 (18)

**Table 2: Cross tabulation of clinical findings with LPC**

Cross tab	LPC		P value
	Positive	Negative	
Clinical finding			
Positive	2	5	0.091
Negative	0	15	

LPC: Leukocyte particle concentration

**Table 3: Cross tabulation of clinical findings with PCR**

Cross tab	PCR		P value
	Positive	Negative	
Clinical finding			
Positive	0	7	1.000
Negative	0	15	

PCR: Polymerase chain reaction

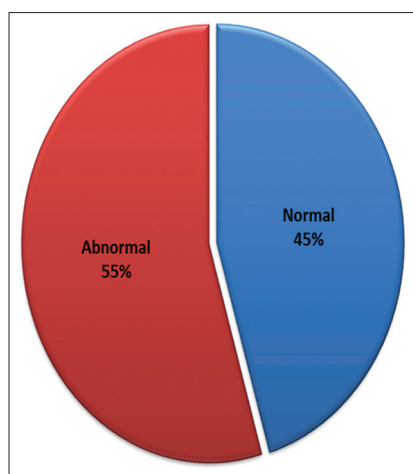


Figure 1: Pervaginal examination findings

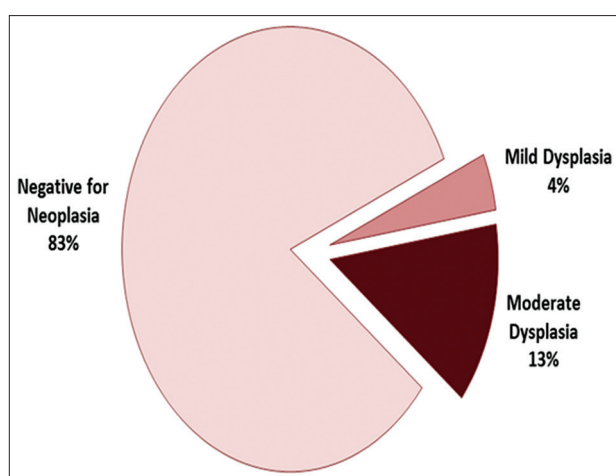


Figure 2: Liquid Pap smear cytology findings

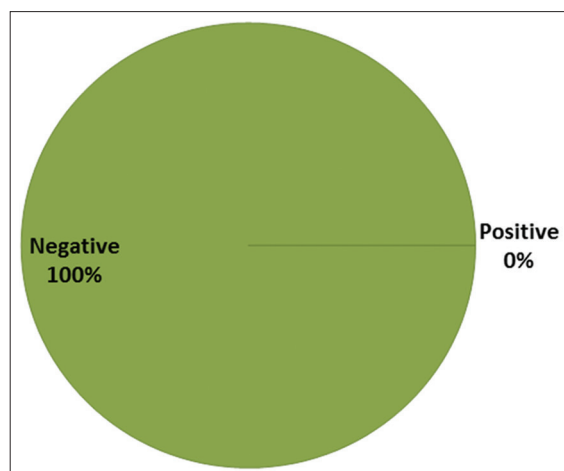


Figure 3: Qualitative human papillomavirus L-1 gene analysis

## DISCUSSION

Currently, in Europe and North America, cervical cancer screening is based on exfoliative cytology performed at

intervals ranging between 1 and 5 years. There has been a marked reduction in incidence and mortality rates of squamous cell carcinoma of the cervix in countries with established cytology screening programs.<sup>12-14</sup>

Cytology had a higher positive predictive value than HPV testing, which reduces the costs associated with referral for colposcopy. However, in well-screened populations, its lower sensitivity is associated with a high proportion of cancers occurring in apparently adequately screened women.<sup>13</sup>

The intent of this study was, if HPV qualitative analysis showed positivity, with a normal Pap smear, then the tests have to be repeated after 1 year as per the recommendations.<sup>15</sup> If Pap smear was abnormal, all these persons require colposcopy and directed biopsy. If there is cervicitis clinically, with normal Pap smear cytology and negative HPV, the tests should be repeated after 1 year and should be under close follow-up.<sup>16</sup>

However, our study showed that qualitative PCR for HPV DNA has very low sensitivity and specificity in clinically symptomatic individuals and liquid Pap smear cytology also showed low detection of CIN lesions in the sample studied.

## CONCLUSION

The results of the above study show that qualitative PCR of the vaginal smear samples for HPV DNA testing does not correlate with liquid Pap smear cytology in clinically symptomatic patients with chronic cervicitis. Hence, quantitative PCR testing is required to stratify the high-risk HPV types.

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# Clinical and Laboratory Profile of Acute Bacterial Meningitis in a Tertiary Care Hospital in Mumbai

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## Abstract

**Introduction:** Acute bacterial meningitis (BM) is a major health concern worldwide, even with the best antimicrobials and available vaccines. A high degree of clinical suspicion, prompt diagnosis, and effective treatment is critical. Laboratory investigations form the cornerstone for correct diagnosis.

**Objectives:** The present study was undertaken to determine the common causative microorganisms of BM and evaluate their antimicrobial susceptibility patterns to establish evidence-based therapeutic strategies.

**Materials and Methods:** Over 1 year, cerebrospinal fluid (CSF) samples from suspected cases of acute pyogenic meningitis were analyzed for biochemical parameters, cell counts, microscopy, and culture on routine and special media. Growth identification and antibiotic susceptibility were performed using standard guidelines.

**Results:** A total of 2326 CSF samples were received, with 111 (4.77%) suggestive of acute pyogenic meningitis. The majority were adults (63%), with male predominance (69.37%). Cases from wards (87.39%) exceeded intensive care units (12.61%). Predominant symptoms/signs were fever (77.48%), neck rigidity (54.05%), and altered sensorium (53.15%). CSF protein value >100 mg/dl and sugar <40 mg/dl were seen in 77.48% and 84.68%, respectively. CSF total leukocyte count >100 cells/ $\mu$ l and polymorphonuclear leukocyte >80% were seen in 92.79% and 51.35%, respectively. On culture, growth was seen in 12.61% samples. Gram-negative bacilli predominated (64.29%). The most common organisms isolated were *Acinetobacter* species (28.57%) and *Streptococcus pneumoniae* (21.43%). *Neisseria meningitidis* and *Haemophilus influenzae* could not be recovered. Gram-positive cocci were 100% susceptible to gentamicin, vancomycin, and linezolid. *S. pneumoniae* isolates were 100% susceptible to penicillin. *Acinetobacter* isolates were 100% susceptible to imipenem. *Enterobacteriaceae* were resistant to amoxicillin-clavulanic acid with 20% susceptibility to cefotaxime and 100% to Imipenem. Paralysis and muscular hypertonia as complications were seen in 2.70% patients. Mortality rate was 5.41% (6/111).

**Conclusion:** BM continues as a public health menace. A combination of clinical and laboratory parameters helps reach the correct diagnosis. Prevailing antimicrobial susceptibility patterns guide effective management.

**Key words:** Antimicrobial susceptibility, Bacterial meningitis, Clinical and laboratory profile

## INTRODUCTION

Bacterial meningitis (BM) is an acute purulent infection within the subarachnoid space often resulting in decreased

consciousness, seizures, raised intracranial pressure, and stroke. The meninges, the subarachnoid space, and the brain parenchyma are all frequently involved in the inflammatory reaction (meningoencephalitis).<sup>1</sup> Meningitis is predominantly aseptic and resolves spontaneously (82-94%), but 6-18% are of bacterial origin.<sup>2</sup> Over 1.2 million cases of BM are estimated to occur worldwide each year.<sup>3</sup> It is the most common and notable infection of the central nervous system, which can progress rapidly and can result in death or permanent debilitation. Not surprisingly, this infection justifiably elicits strong emotional responses and hopefully immediate medical intervention.<sup>4,5</sup>

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It is much more common in developing countries than developed countries.<sup>4,5</sup> Many factors predispose to BM including age, male gender, winter season, smoking and exposure to smokers, low socioeconomic status, and stress.<sup>6</sup> Congenital anomalies or injury to the central nervous system and primary infection elsewhere, especially that adjacent to the meninges are other well-established predisposing factors.<sup>7</sup>

BM is caused by a number of organisms, the most common being *Streptococcus pneumoniae* (*S. pneumoniae*), *Neisseria meningitidis*, and *Haemophilus influenzae*.<sup>4,7-9</sup> *H. influenzae* Type b (Hib) used to be a common cause of BM worldwide before the Hib vaccines. Over the last two decades, however, the causative agents of meningitis have changed with the introduction of new highly effective vaccines.<sup>10</sup> More recently, *S. pneumoniae* and *N. meningitidis* have become the predominant organisms causing meningitis. In countries with high HIV prevalence, *Cryptococcus neoformans* may also be significant.<sup>9</sup>

The most common neurological complication of BM is hearing impairment, especially with *S. pneumoniae*.<sup>11</sup> Other complications include subdural effusions, subdural empyema, brain abscesses, seizure, disseminated intravascular coagulation, shock, and mortality. Children may develop neuromotor and learning disabilities, speech and behavioral problems.<sup>12</sup>

Before the introduction of antibiotics in the 1940s, case fatality rates for epidemic and endemic BM exceeded 70%. Since then, antibiotic use has reduced case fatality rates of the same to  $\leq 25\%$ .<sup>13</sup> However, both the morbidity and the mortality of untreated and inappropriately treated BM patients remain high.<sup>7,8</sup> In economically advanced countries, the mortality from BM is  $<10\%$ , but it may be  $\geq 30\%$  in developing countries.<sup>6</sup> Majority of patients with BM survive, but neurological sequelae occur in 10-35% of all survivors (especially newborns and children).<sup>12</sup>

Microbiology laboratories and the microbiologists play a critical role not only in the early identification of the causative bacteria and their antibiotic susceptibility pattern but also in providing valuable information regarding the common pathogens prevalent in a particular area.<sup>3,13</sup> Regional information regarding changing trends in etiology of meningitis and antimicrobial susceptibility pattern is essential for correct and timely management of meningitis. Microbiology laboratories are the foundation of public health surveillance for BM<sup>3</sup> and are guides to the clinicians for starting empiric as well as specific therapies.

Several published studies of acute BM are available from the developed countries,<sup>10,14-16</sup> but there is paucity of

data regarding the same in the developing countries like India.<sup>13,17-19</sup>

Therefore, the present study was undertaken to determine the common microorganisms responsible for BM in a tertiary care hospital in Mumbai, to evaluate the antimicrobial susceptibility pattern of microorganisms isolated from the cerebrospinal fluid (CSF) samples and to establish evidence-based therapeutic strategies for the treatment of BM.

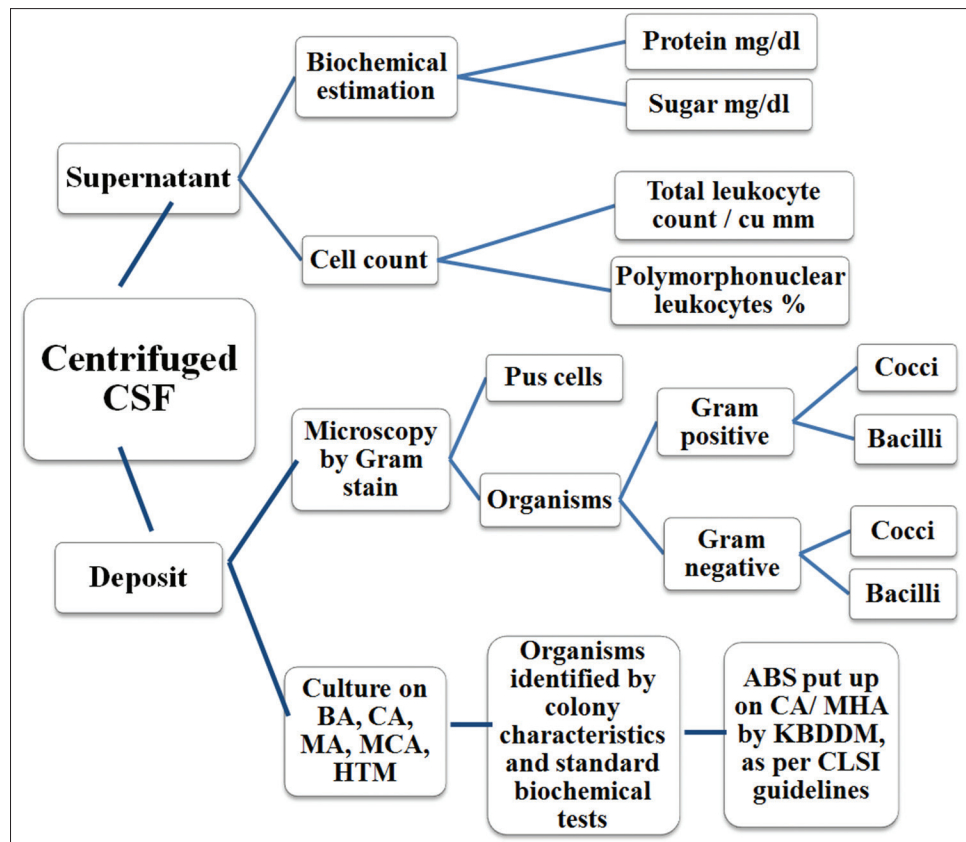
## MATERIALS AND METHODS

This was a prospective study carried over 1 year (from June 2012 to May 2013) in a tertiary care hospital in Mumbai, with institutional ethical clearance. 111 consecutive patients admitted with signs and symptoms of acute pyogenic meningitis and of any age and gender were included in this study. Exclusion criteria were patients without any signs and symptoms of acute pyogenic meningitis, HIV seropositive patients and patients not willing to participate in the study.

A written informed consent was taken from the patient (or the relatives/guardians, in case of unconscious patients and children). A detailed clinical history and a thorough physical examination were done and a pro forma filled up, recording all the relevant details.

CSF samples from each patient were collected using sterile, aseptic technique. Around 2 ml of CSF was taken into two sterile test tubes for cell counts, biochemical parameters and bacterial culture studies. CSF from both the sterile culture tubes was centrifuged at 1500 rpm for 15 min. The supernatant from the first tube was used for total cell count, differential count, and sugar and protein estimation. Around 0.5 ml of the deposit from the first tube was utilized for Gram-staining. The deposit from the second tube was divided into two parts. One part was processed by a conventional method on blood agar (BA), chocolate agar (CA), and MacConkey agar (MA). BA and CA were incubated at 37°C in a candle jar at 5% CO<sub>2</sub> atmosphere for 48 h. MA was incubated at 37°C for 18-24 h. The other part was plated on modified CA (MCA) incorporated with isovitalex and vitamin K2 and incubated at 37°C at 5% CO<sub>2</sub> atmosphere for 48 h (Figure 1). The remaining CSF was kept in the incubator at 37°C as a backup for potential reculture.<sup>20</sup> All isolates grown were identified by colony characteristics and standard biochemical tests.<sup>21</sup>

Antimicrobial susceptibility test was performed for each of the isolates by Kirby-Bauer Disc Diffusion Method (KBDDM). The media used were *Haemophilus* test medium (HTM) for *H. influenzae* and Mueller-Hinton agar (MHA)



**Figure 1:** Flow chart of processing of CSF samples. CSF: Cerebrospinal fluid; BA: Blood agar; CA: Chocolate agar; MA: MacConkey agar; MCA: Modified chocolate agar; HTM: Haemophilus test medium; MHA: Mueller Hinton agar; ABS: Antibiotic susceptibility test; KBDDM: Kirby-Bauer Disc Diffusion Method; CLSI: Clinical and Laboratory Standards Institute

with 5% sheep blood for *S. pneumoniae* and *N. meningitidis*. For other bacteria, MHA was used for antimicrobial susceptibility testing by KBDDM. Appropriate control strains were used. The agar plates were incubated at 35°C for 18 h, and antimicrobial susceptibility pattern was interpreted as per the Clinical and Laboratory Standards Institute guidelines, 2012.<sup>22</sup>

The data from each patient were compiled on the Microsoft Excel sheet by OpenEpi software version 2.3. The quantitative data were expressed as mean  $\pm$  standard deviation (SD).

## RESULTS

A total of 2326 CSF samples were received in the laboratory, of which, 111 were cases of acute pyogenic meningitis, indicating a prevalence of 4.77% in this tertiary care hospital. The majority of cases were seen among adults (63.06%), with an adult to child ratio of 1.71:1. Males (69.37%) were affected more than females with male to female ratio of 2.26:1. Among the pediatric patients, maximum number of cases were in the age group of 0-2 years (58.5%). Among the adults, maximum number of cases were in the age group of 16-40 years (67.1%).

Almost 87.39% (97/111) of the cases were from wards and only 14 cases (12.61%) were from intensive care units (ICUs). Among ICUs, maximum cases were from pediatric intensive care unit (42.9%), and among wards, maximum cases were from adult medicine wards (62.89%), followed by pediatric medicine wards (26.80%). Cases from ICU areas were more in children, i.e., 11 (9.91%), in comparison to adults, i.e., 3 (2.7%), whereas in wards, the majority of the cases were from adults, i.e., 67 (60.36%).

Maximum cases presented with fever, i.e., 86 (77.48%), followed by neck rigidity in 60 (54.05%), altered sensorium in 59 (53.15%), headache in 46 (41.4%), and vomiting in 40 (36.04%) cases. The different combinations of the presenting symptoms and signs were analyzed. Maximum patients presented with fever and altered sensorium (9.01%), followed by fever, headache, and neck rigidity (7.21%). Combination of 2 or 3 signs/symptoms were seen in 36 (32.43%) cases.

Of the predisposing factors, post-operative status was the most common (4.5%), followed by trauma (3.6%). In the majority of the cases (89.2%), predisposing factor could not be identified.

Mean  $\pm$  SD of CSF protein was  $309.16 \pm 400.10$  mg/dl. Maximum cases (34.24%) had CSF protein values between 101 and 200 mg/dl. CSF protein value  $>100$  mg/dl was seen in 77.48% cases.

Mean  $\pm$  SD of CSF sugar was  $28.17 \pm 16.52$  mg/dl. Maximum cases (72.07%) had CSF sugar values between 11 and 40 mg/dl. CSF sugar value  $< 40$  mg/dl was seen in 84.68% cases.

Mean  $\pm$  SD of CSF total leukocyte count (TLC) was  $1057.72 \pm 1871.86$  cells/ $\mu$ l. Maximum cases (49.55%) had CSF TLC between 101 and 500 cells/ $\mu$ l. CSF TLC  $>100$  cells/ $\mu$ l was seen in 92.79% cases.

Mean  $\pm$  SD of CSF polymorphonuclear (PMN) leukocytes was  $74.41 \pm 20.10\%$ . Maximum cases (51.35%) had CSF PMN leukocytes between 81% and 100%. CSF PMN leukocytes  $>40\%$  was seen in 90.1% cases.

In 87.4% CSF samples, pus cells could be seen on microscopy after Gram-stain. 10.8% CSF samples showed Gram-stained microorganisms. Gram-negative organisms predominated (66.67%) and the rest were Gram-positive organisms (33.33%). In 89.2% CSF samples, no organisms were detected on Gram-stain.

Growth was seen in 14 samples (12.61%) and contamination was noted in 4 (3.61%) samples (three with micrococci and one with diphtheroids). No growth was seen in 83.78% samples. Gram-negative bacilli were grown in 64.29% and Gram-positive cocci in 35.71% cases. The most common organism isolated was *Acinetobacter* species (28.57%), followed by *S. pneumoniae* (21.43%) (Table 1).

All the three *S. pneumoniae* isolates were susceptible to penicillin, gentamicin, trimethoprim-sulfamethoxazole (TMP-SMX), cefuroxime, vancomycin, and linezolid. One methicillin-resistant *S. aureus* (MRSA) was sensitive to gentamicin, vancomycin, and linezolid. One methicillin-sensitive *S. aureus* (MSSA) was sensitive to gentamicin and TMP-SMX.

All *Acinetobacter* isolates were susceptible to imipenem. Piperacillin-tazobactam (PIT) and netilmicin susceptibility was seen in 75% isolates of *Acinetobacter*. None of the isolates was susceptible to cefotaxime (Table 2). All *Enterobacteriaceae* were susceptible to imipenem. Susceptibility to ciprofloxacin, PIT, and netilmicin was 60% each. Amikacin (AK), cefotaxime, and piperacillin susceptibility was only 20% each. None of the isolates was susceptible to amoxicillin-clavulanic acid. No carbapenem resistance was detected (Table 2).

Among complications, paralysis and muscular hypertonia each were seen in 2.70% patients. No complications were seen in 94.6% cases.

Overall, mortality rate was 5.41% (6/111). Out of six cases, one was culture positive for *Acinetobacter* species and in five cases cultures were negative.

## DISCUSSION

This study was aimed at understanding the clinical and laboratory profile of BM. Although the disease continues to be a major public health concern, there is no single parameter that can define the illness and the outcome. The isolation of the causative organism and confirmation by culture continues to be the gold standard for diagnosis.

The disease prevalence in this hospital was 4.77% (111/2326), with 63% of the affected being adults. Studies

**Table 1: Organisms isolated from CSF in cases of acute pyogenic meningitis**

Organism	n (%)
<i>S. pneumoniae</i>	3 (21.43)
<i>N. meningitidis</i>	0 (0)
<i>H. influenza</i>	0 (0)
<i>Acinetobacter</i> species	4 (28.57)
<i>Klebsiella pneumoniae</i>	1 (7.14)
<i>Escherichia coli</i>	1 (7.14)
<i>Enterobacter aerogenes</i>	2 (14.30)
<i>Salmonella typhi</i>	1 (7.14)
MRSA	1 (7.14)
MSSA	1 (7.14)
Total	14 (100)

CSF: Cerebrospinal fluid. *S. pneumoniae*: *Streptococcus pneumoniae*, *N. meningitidis*: *Neisseria meningitidis*, *H. influenzae*: *Haemophilus influenzae*, *Klebsiella pneumoniae*: *K. pneumoniae*, *E. coli*: *Escherichia coli*, *E. aerogenes*: *Enterobacter aerogenes*, *S. typhi*: *Salmonella typhi*. MRSA: Methicillin-resistant *Staphylococcus aureus*, MSSA: Methicillin-sensitive *Staphylococcus aureus*

**Table 2: Antimicrobial susceptibility pattern of Gram-negative bacilli isolated from CSF**

Antibiotic	<i>Acinetobacter</i> species (n=4) (%)	<i>Enterobacteriaceae</i> (n=5) (%)
AK	2 (50)	1 (20)
CIP	1 (25)	3 (60)
CTX	0 (00)	1 (20)
PI	2 (50)	1 (20)
AMC	1 (25)	0 (00)
IPM	4 (100)	5 (100)
CPM	1 (25)	1 (20)
NET	3 (75)	3 (60)
PIT	3 (75)	3 (60)
CIS	2 (50)	1 (20)
CAS	2 (50)	1 (20)

AK: Amikacin, CIP: Ciprofloxacin, CTX: Cefotaxime, PI: Piperacillin, AMC: Amoxicillin-clavulanic acid, IPM: Imipenem, CPM: Cefepime, NET: Netilmicin, PIT: Piperacillin-Tazobactam, CIS: Ceftriaxone-Sulbactam, CAS: Ceftazidime-Sulbactam, CSF: Cerebrospinal fluid

from South India<sup>19</sup> and Niger<sup>5</sup> have reported 86.8% and 70% adult population, respectively, among their patients. Males predominated (69.37%) in this study. Almost all studies have shown male preponderance.<sup>5,19,23</sup>

Among children, 58.5% of the cases were in the age group of 0-2 years and 80.5% cases were below 5 years of age, together contributing to 30% of all cases of meningitis. Studies from Niger<sup>5</sup> and India<sup>24</sup> have reported 42.2% and 66.67% cases, respectively, in children below 5 years of age. A major risk factor for meningitis is the lack of immunity to specific pathogens associated with young age. Incidence of meningococcal disease increases in infants <1 year old, and this may be attributable to immature alternative and lectin complement pathways and lack of acquired serum antibodies.<sup>25</sup>

Among 111 cases of acute pyogenic meningitis, fever was the most common symptom (77.5%), followed by neck rigidity (54%), altered sensorium (53%), and headache (41.4%). Thomas *et al.*<sup>26</sup> have also reported fever, neck rigidity, and headache in 71%, 48%, and 92% cases, respectively. van de Beek *et al.*<sup>15</sup> have reported neck rigidity in 83%, headache in 87%, and altered sensorium in 69% of their cases, which are much higher as compared to this study. Convulsions were seen to the extent of 9.9% in this study. Thomas *et al.*<sup>26</sup> and van de Beek *et al.*<sup>15</sup> have reported figures of 9% and 15%, respectively, in their studies. However, Mwaniki *et al.*<sup>27</sup> have reported convulsion in 38.7% cases. Kernig's/Brudzinski's sign was seen in 10% cases in this study as compared to 5% reported by Thomas *et al.*<sup>26</sup> The classic triad of acute pyogenic meningitis includes fever, neck stiffness, and altered sensorium.<sup>15</sup> In this study, classic triad was present in 1.8% of the cases. At least two of the four signs (classic triad + headache) were present in 21.6% of the cases. Any one of the four signs and symptoms was present in 10.8% of the cases. All four were present in 5.4% of the cases. van de Beek *et al.*<sup>15</sup> have reported 44% of cases characterized by classic triad, 95% presenting with at least two of the four signs/symptoms and 4% with any one of the four.

In this study, maximum patients presented with fever and altered sensorium (9%), followed by fever, headache, and neck rigidity (7.2%). Combinations of 2 and 3 signs/symptoms were maximum (32.4% each). Thomas *et al.*<sup>26</sup> have reported a combination of fever, headache, vomiting, photophobia, and neck rigidity as maximum. Post-operative status was the commonest predisposing factor (4.5%), followed by trauma in 3.6% cases.

CSF examination of a normal adult shows TLC <5 cells/ $\mu$ l (in case of newborns, TLC is <20 cells/ $\mu$ l) with no PMN leukocytes. Normally, CSF glucose and protein value in a healthy person is  $\geq 45$  mg/dl and <40 mg/dl, respectively.<sup>1</sup>

Different authors have reported CSF TLC >79 cells/ $\mu$ l in their cases.<sup>15,16,19,28</sup> The present study had TLC >100 cells/ $\mu$ l in 92.79% cases and CSF TLC between 101 and 500 cells/ $\mu$ l in 49.55% cases. TLC as high as >1000 cells/ $\mu$ l was seen in 25.22% cases and a low TLC <100 cells/ $\mu$ l was seen in 7%. Although high TLC is a marker of acute BM, Lussiana *et al.*<sup>28</sup> Mani *et al.*<sup>19</sup> have reported even <10 cells/ $\mu$ l in some cases. In this study, mean  $\pm$  SD of TLC was  $1057.72 \pm 1871.86$  cells/ $\mu$ l. Thomas *et al.*<sup>26</sup> have reported TLC Mean  $\pm$  SD of  $359 \pm 1543$  cells/ $\mu$ l. A predominance of lymphocytes also occurs in some cases, as is also seen in this study in 11 cases, where PMN leukocytes were <40%. A marker of BM is the presence of >80-85% of PMN leukocytes in CSF,<sup>8,29</sup> and this study reported PMN leukocytes >80% in 51.35% cases. The Mean  $\pm$  SD of CSF PMN leukocyte % was  $74.41 \pm 20.10\%$  in this study.

In this study, CSF sugar <40 mg/dl was seen in 84.68% cases. Studies by Wu *et al.*<sup>16</sup> and Lussiana *et al.*<sup>28</sup> have reported the same in 30% and 74%, respectively. In this study, mean  $\pm$  SD of CSF sugar was  $28.17 \pm 16.52$  mg/dl which is similar to the mean  $\pm$  SD  $31.15 \pm 22.37$  mg/dl reported by Lussiana *et al.*<sup>28</sup>

CSF protein >100 mg/dl was seen in 77.48% cases in this study. Other studies have reported >85% cases with high CSF protein value.<sup>26,28</sup> However, Wu *et al.*<sup>16</sup> have reported only 53.7% cases with CSF protein >100 mg/dl. Mean  $\pm$  SD of CSF protein in this study was  $309.16 \pm 400.10$  mg/dl. van de Beek *et al.*<sup>15</sup> have reported high protein Mean  $\pm$  SD of  $490 \pm 450$  mg/dl.

Pus cells were seen on Gram-stain from the centrifuged deposit of CSF (1500 revolutions per minute for 15 min) in 87.4% cases. However, organisms were seen only in 12 samples (10.8%) on Gram-stain. Gram-positive cocci were seen in four cases, Gram-negative cocci in two cases and Gram-negative bacilli in six. In 89.2% CSF samples, no organisms were detected on Gram-stain. A relatively high yield of organisms on Gram stain can be obtained using Cytospin as seen in studies by Mani *et al.*<sup>19</sup> (65.7% with cytopspin at 800 revolutions per minute for 10 minutes) and Shanholtzer *et al.*<sup>30</sup> (75% with cytopspin at 2000 revolutions per minute for 10 minutes). Low positivity in this study can be attributed to not using cytopspin to concentrate the smear for Gram-stain. Wu *et al.*<sup>16</sup> have reported a predominance of Gram-positive organisms (69.4%) on Gram-stain, whereas the present study had predominance of Gram-negative organisms (66.67%).

Among 111 CSF samples, organisms could be recovered on culture in only 14 (12.6%) cases. No growth was seen in 83.8% of the samples. Wu *et al.*<sup>16</sup> have shown culture positivity of 22.2%. Several studies have reported a low

CSF culture positivity, ranging from 3.3% to 45.5%.<sup>5,9,18,19</sup> In this study, contamination was seen in four samples (three micrococci and one diphtheroids), which may be due to improper aseptic precautions while performing lumbar puncture.

*S. pneumoniae* was isolated from 21.43% of culture positive samples. Overall culture positivity of *S. pneumoniae* in various studies varies from as low as 2.4% from Bengaluru<sup>18</sup> to as high as 77% from Ghana.<sup>9</sup>

This study failed to recover *N. meningitidis* and *H. influenzae* even though selective media such as MCA and HTM were used for these fastidious organisms (Table 1). Isolation of *N. meningitidis* in CSF is very low in India, 1% from Bengaluru,<sup>18</sup> and varying from 1% to 25% in western countries.<sup>9,10,16</sup> A study from Niger<sup>5</sup> had high isolation rate (63%) of *N. meningitidis* from CSF.

The *H. influenzae* Type b (Hib) study working group has reported a high culture positivity of *H. influenzae* (34.62%).<sup>31</sup> In all other studies, *H. influenzae* positivity rate varied from 0.9% to 12.6%.<sup>5,10,16,19</sup> The incidence of *H. influenzae* disease has remained low for the past several decades in India and vaccination of Hib, though not included in national immunization program, is recommended by the Indian Academy of Pediatrics and World Health Organization (WHO), for all children below 6 years of age with 3 doses at 6, 10, and 14 weeks.<sup>32</sup>

Campagne *et al.*<sup>5</sup> have reported that 80% cases of BM were caused by the three bacteria *S. pneumoniae*, *N. meningitidis*, and *H. influenzae*. However, in this study, Gram-negative bacilli predominated (64.29%). Mwaniki *et al.*<sup>27</sup> have reported 24.5% Gram-negative bacilli from culture positive cases of CSF. Other studies have reported lesser isolation of Gram-negative bacilli in the range of 2.4–8.3%.<sup>9,16,19</sup>

Three common causes of neonatal meningitis are Group B *Streptococcus*, *Listeria monocytogenes*, and *Escherichia coli*.<sup>33</sup> However, we did not encounter any case of Group B *Streptococcus* or *L. monocytogenes*, but one *E. coli* was isolated from a CSF sample of an adult male. A study from Atlanta,<sup>10</sup> in 1997, has reported both the above organisms, and a recent study<sup>16</sup> from the same country, in 2013, has also reported *Listeria* in 0.2% cases. From Chennai, a case of *L. monocytogenes* has been reported from a CSF of 17-year-old girl.<sup>34</sup> In the present study, one *Salmonella typhi* was isolated from CSF of a 4-month-old female child in this study. *Salmonella* species and *Flavobacterium meningosepticum* meningitis have been reported earlier in cases of acute meningitis from Bengaluru.<sup>19</sup>

The most common organisms of nosocomial meningitis are Coagulase-negative *Staphylococcus*, *Acinetobacter* species, and *S. aureus*.<sup>35</sup> This study isolated four *Acinetobacter* species of which three were male children and one, a young adult male. The latter was a post-operative case of neurosurgery. Of these, one child expired (25% mortality due to *Acinetobacter*). *Acinetobacter* species are becoming increasingly important as nosocomial pathogens and *Acinetobacter* meningitis typically occur the following neurosurgery, with mortality exceeding 15%.<sup>36</sup>

Low yield of bacteria on culture may be due to prior antibiotic use as most patients take antibiotics from private practitioners or over the counter as community antibiotic use is very prevalent in India.<sup>31</sup> Other reasons are delay in the transport of sample to the laboratory, nonavailability of selective/special media for the fastidious pathogens, presence of autolytic enzymes in CSF, and a lack of 24-h facility for processing of CSF samples.<sup>19</sup> This hospital, however, has 24-h emergency services and also selective media were used for culture.

All three *S. pneumoniae* isolates were susceptible to penicillin, cefuroxime, gentamicin, linezolid, and vancomycin. In a study from Bengaluru,<sup>19</sup> all *S. pneumoniae* isolates were sensitive to penicillin and vancomycin. Although high-level resistance (24%) to TMP-SMX was reported in invasive pneumococcal infections from South India,<sup>24</sup> in this study, all *S. pneumoniae* isolates were susceptible to TMP-SMX. Jain *et al.* from Delhi have reported high TMP-SMX resistance and low penicillin resistance in pneumococcal isolates.<sup>37</sup>

Two *S. aureus* isolated: One MSSA and another one MRSA were 100% susceptible to gentamicin. The MRSA was also susceptible to vancomycin and linezolid. No vancomycin-intermediate *S. aureus* and vancomycin-resistant *S. aureus* (VRSA) were detected. In the present study, no *Enterococcus* species was isolated. A study from Aligarh<sup>13</sup> has reported increase in the prevalence of MRSA causing meningitis from 44.4% in 2005 to 69.4% in 2008–2009 and increase in high-level aminoglycoside resistance among *Enterococcus faecalis* isolates from 52.9% in 2005 to 60% in 2008–2009. However, no VRSA or vancomycin-resistant *Enterococcus* was encountered in that study.

An outbreak due to *N. meningitidis* serogroup A in Delhi, in 2007, have reported decreased susceptibility of these isolates to ciprofloxacin (only 14.3%).<sup>23</sup> Furthermore, resistance to ampicillin and chloramphenicol is common among *H. influenzae* isolates and seems to be increasing.<sup>5</sup> However, in this study, *N. meningitidis* and *H. influenzae* could not be recovered from CSF culture, and thus, antibiotic susceptibility cannot be commented upon.

Currently in India, the third generation cephalosporin is the drug of choice for management of invasive pneumococcal and *H. influenzae* diseases.<sup>37</sup> In addition, vancomycin should be added in invasive pneumococcal infection. Alternative therapy for *S. pneumoniae* is meropenem/fluoroquinolone. Alternative therapy for *N. meningitidis* and *H. influenzae* are chloramphenicol/fluoroquinolone. In addition, penicillin G/ampicillin can also be given in meningococcal meningitis.<sup>33</sup>

Out of *Acinetobacter* species isolated from CSF in this study, 50% were susceptible to AK and piperacillin and only 25% to ciprofloxacin and amoxicillin-clavulanic acid. They were 75% susceptible to piperacillin-tazobactam and netilmicin and 100% susceptible to imipenem. Cefotaxime susceptibility was 0% (Table 2). *Acinetobacter* species are frequently resistant to cephalosporins such as cefepime or ceftazidime, and in carbapenem-resistant isolates, this resistance goes up to 95%. Therefore, these cephalosporins are less useful as empirical agents in patients from neurosurgical units, where *Acinetobacter* meningitis is common.<sup>36</sup> Although AK susceptibility in this study was 50%, poor penetration of aminoglycoside through the blood brain barrier does not suggest intravenous administration in the treatment of meningitis. Therefore, aminoglycoside has to be administered by intraventricular route.<sup>36</sup>

In this study, among the first line antibiotics, susceptibility of *Enterobacteriaceae* was 60% to ciprofloxacin and 20% each to AK, cefotaxime, and piperacillin. Susceptibility to amoxicillin-clavulanic acid was 0%. However, all *Enterobacteriaceae* were 100% susceptible to imipenem, followed by 60% to piperacillin-tazobactam and netilmicin (Table 2). Therefore, no carbapenem resistance was detected. A recent study from Aligarh,<sup>13</sup> in 2011, has reported aminoglycoside susceptibility to be as high as 75%, followed by 69% to cefotaxime in. Fluoroquinolone susceptibility of 62.5% and imipenem susceptibility of 100% is almost similar to the present study (60% and 100%, respectively). Mani *et al.*<sup>19</sup> have reported 73.7% susceptibility to AK, 47.4% to cefotaxime, and 52.6% to ciprofloxacin.

No complications were seen in the majority of the cases (95%) in this study. The common complications seen in cases of acute pyogenic meningitis are cranial nerve palsy, hemiparesis/quadruparesis, stroke, cerebral/cerebellar herniation, and thrombosis of dural venous sinuses.<sup>25</sup> In this study, overall complications seen were paralysis and muscular hypertonia in 2.7% patients each. van de Beek *et al.*<sup>15</sup> have reported cranial nerve palsy in 19% of their cases, paralysis in 5%, and aphasia in 2%. However, none of the patients developed cranial nerve palsy or aphasia in this study.

In this study, 6 out of 111 cases of acute pyogenic meningitis expired with an overall mortality rate of 5.41%. Various studies have reported mortality rate in acute pyogenic meningitis cases ranging from 10% to 31.3%.<sup>5,13,15-17,28,31</sup> Antibiotic usage has definitely reduced the case fatality rate of acute pyogenic meningitis to 25% or less, with a few exceptions.<sup>13</sup> Mortality due to *S. pneumoniae* in children <5 years of age has been reported to be as high as 73% by the WHO.<sup>3</sup> Kanungo *et al.*<sup>24</sup> from Pondicherry have reported mortality of 20% in meningitis due to *S. pneumoniae*. In this study, mortality due to *S. pneumoniae* meningitis was seen in 25% (2/8 cases). Small scale studies from India have documented case fatality rate for meningitis due to *H. influenzae* Type b to be 11%.<sup>17</sup> In this study, *H. influenzae* could not be isolated by culture and thus cannot be commented upon. A 65-year-old male patient admitted with high-grade fever, vomiting, altered sensorium, and a known case of chronic obstructive pulmonary disease and who was culture negative, died due to raised intracranial tension due to tuberculous meningitis.

## CONCLUSION

BM continues to be a public health menace. Although the prevalence of the various causative agents varies with age and the geographical area, *S. pneumoniae*, *H. influenzae* Type b, and *N. meningitidis* are reported by many researchers to be the main pathogens of acute pyogenic meningitis.

A combination of clinical and laboratory parameters need to be taken into consideration to arrive at the right diagnosis. Emergence of resistant bacterial strains to conventional antibiotics warrants the need to consider the prevailing antimicrobial susceptibility patterns for the effective management of the disease. This also helps in formulating the local treatment guidelines and acts as a proactive public health surveillance system.

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# Correlation between Glycated Hemoglobin and Dyslipidemia in Patients with Type 2 Diabetes Mellitus in a Tertiary Care Hospital, Maharashtra, India

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## Abstract

**Introduction:** Dyslipidemia is one of the major risk factors for cardiovascular disease in diabetes mellitus Type 2. The aim of the study was to understand the pattern of dyslipidemia among the Type 2 diabetic patients and to understand its association with glycated hemoglobin (HBA1C).

**Materials and Methods:** This is a retrospective cross-sectional study carried out in KIMS, Karad, Maharashtra, India, to assess the relationship between glycemic control (as reflected by HBA1C) and serum lipid profile in Type 2 diabetic patients which included a total of 100 Type 2 diabetic patients (54 males; 46 females; mean age years). Venous blood samples were collected from all the patients after at least 8 h fasting.

**Results:** The sera were analyzed for HBA1C, fasting blood glucose (FBG), total cholesterol, triglycerides (TG), high-density lipoprotein (HDL) cholesterol, and low-density lipoprotein (LDL) cholesterol. The levels of HBA1C, FBG, and LDL did not differ significantly between males and females. Female patients showed significantly higher serum cholesterol and HDL but significantly lower TG levels as compared to males. There was a highly significant correlation between HBA1C and FBG. Both HBA1C and FBG exhibited direct correlations with cholesterol, TG, and LDL and inverse correlation with HDL; the magnitude of significance for all these lipid parameters being greater with HBA1C than FBG. There was a linear relationship between HBA1C and dyslipidemia. The levels of serum cholesterol and TG were significantly higher and of HDL significantly lower in patients with worse glycemic control as compared to patients with good glycemic control.

**Conclusion:** The findings of this study clearly showed that HBA1C is not only a useful biomarker of long-term glycemic control but also a good predictor of lipid profile.

**Key words:** Cholesterol, Diabetes mellitus, Dyslipidemia, Glycated hemoglobin, High-density lipoprotein cholesterol, Low-density lipoprotein cholesterol, Triglycerides

## INTRODUCTION

Dyslipidemia is one of the major risk factors for cardiovascular disease in diabetes mellitus Type 2.<sup>1,2</sup> The aim of the study was to understand the pattern of dyslipidemia among the Type 2 diabetic patients and to understand its association with Glycated hemoglobin (HBA1C).

It is estimated that currently India has 62.4 million people with diabetes mellitus. This is a major public health challenge, and it is increasing in epidemic proportions. Chronic hyperglycemia leads to micro- and macro-vascular complications. The lipid abnormalities in diabetics such as increased cholesterol, increased LDL, high triglycerides (TG), and low high-density lipoprotein (HDL) are contributing to the mortality and morbidity. Worsening of glycemic control deteriorates lipid and lipoprotein abnormalities and particularly of diabetes mellitus. The combination of hyperglycemia, dyslipidemia, and hypertension produces enhanced atherogenic environment within the circulation. This leads to increased risk of ischemic heart disease, stroke, and myocardial infarction. Diabetes mellitus is considered as coronary heart disease

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equivalent. Insulin resistance, relative insulin deficiency, and obesity are associated with deranged lipid profile. The American Diabetes study has come to a conclusion that HBA1C <7 mg/dl signifies optimal blood glucose levels. The management should focus on controlling diabetes and managing lipid levels which will reduce mortality and morbidity for ischemic heart disease and other diabetic complications.<sup>2,3-10</sup>

HBA1C is routinely measured to check the glycemic control over a preceding 8-12 weeks of time. It is used as an indicator for the state of glycemic control. Progression of the disease and the development of the complications in diabetic patients. The aim of the study was to examine the impact of the glycemic control on the lipid profile of Type 2 diabetic patients and to know the importance of HBA1C as an indirect indicator of dyslipidemia.

## MATERIALS AND METHODS

- Design of the study - Retrospective cross-sectional descriptive study
- Duration of the study - The study was carried out on diabetic patients during 6-month period from 1<sup>st</sup> January 2016 to 31<sup>th</sup> June 2016
- Source of the data - History, physical examination, laboratory investigations were obtained from the medical records department
- Method of collection of data - Total of 100 patients records were accessed from the medical records department in KIMS Karad.

### Inclusion Criteria

All diagnosed cases of Type 2 diabetes mellitus.

### Exclusion Criteria

- Age below 18 years
- Type 1 diabetics
- Patients on lipid lowering agents
- Acute coronary syndrome
- Stroke.

The lipid profile of the study was analyzed according to the ATP III classification for identification of dyslipidemia, Low HDL <40 mg/dl.

High low-density lipoprotein (LDL) >190 mg/dl, high cholesterol >200 mg/dl, and high TG >200 mg/dl.

## RESULTS

A total of 100 patients with Type 2 diabetes mellitus were followed (52 males and 48 females) (Figure 1). The mean

**Table 1: Demographic data of diabetes mellitus**

Number of cases	100
Male	52
Female	48
Mean age of year	62.91
Age range (year)	30-85

**Table 2: Lipid profile and HBA1C of diabetic patients**

Parameter	Mean±SD
Total cholesterol	149.73±47.37
TG	173.27±53.61
LDL	65.86±54.27
HDL	38.61±15.45
HBA1C	8.92±2.24

TG: Triglyceride, LDL: Low-density lipoprotein, HDL: High-density lipoprotein, HBA1C: Glycated hemoglobin, SD: Standard deviation

**Table 3: Frequency of abnormal lipid profile status in all patients**

Dyslipidemia	Total	Male	Female
Hypercholesterolemia	36	17	19
Hypertriglyceridemia	32	14	18
low HDL-C	60	33	27
high LDL-C	8	3	5
No abnormal lipid profile	16	9	6
One abnormal lipid profile	45	20	25
Two abnormal lipid profile	28	14	14
>Two abnormal lipid profile	11	4	7

LDL-C: Low-density lipoprotein cholesterol, HDL-C: High-density lipoprotein cholesterol

age was 62.91 years with age range of 30-85 years (Table 1). Poor glycemic control (HBA1C >8) was seen in 62% of total patients. Poor glycemic control was associated with dyslipidemia in 41.5% of total patients, whereas 20.5% accounted for poor glycemic control without dyslipidemia, the maximum frequency of abnormal lipid profile status in all patients was low LDL cholesterol (LDL-C) (Tables 2 and 3) and the age group with maximum patients with both dyslipidemia and higher HBA1C levels was 51-60 years.

## DISCUSSION

In our study conducted in a tertiary health-care center in Maharashtra, India, the lipid profile, fasting blood glucose (FBG), and HBA1C were investigated. A total number of 100 patients were included in the study. Abnormality of cholesterol metabolism may lead to cardiovascular disease and heart attacks. This study reveals a high prevalence of hypercholesterolemia, hypertriglyceridemia, high LDL, and low HDL levels which are well-known risk factors for cardiovascular disease and incidence of poor glycemic control in Type 2 diabetic patients. Insulin affects the liver

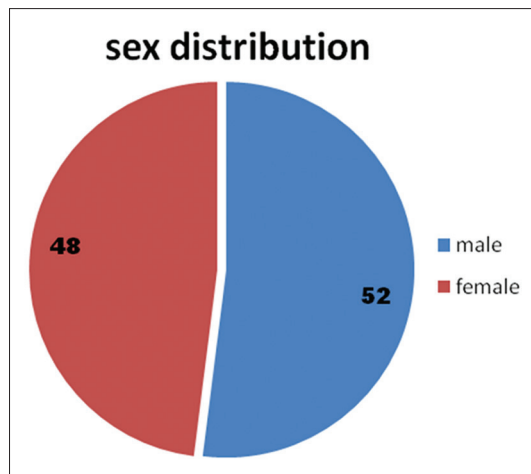


Figure 1: Sex distribution among study population

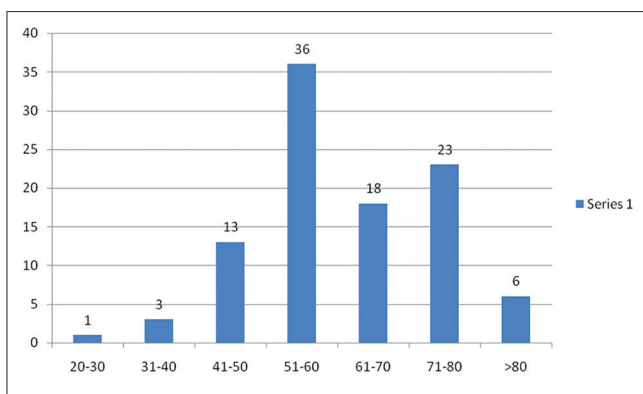


Figure 2: Age distribution among the study population

Apo-lipoprotein production. It regulates the enzymatic activity of lipoprotein lipase and cholesterol ester transfer protein. All these factors are likely cause of dyslipidemia in diabetes mellitus [11]. Worse glycemic control with dyslipidemia was seen maximum in the individual of the age group 51-60 years (Figure 2). The core of this study revolved around identification of an association between dyslipidemia and poor glycemic control. The percentage of dyslipidemic individuals among the study population amounted to 62%, among which 41.5% accounted for dyslipidemia with poor glycemic control (HBA1C >8 mg/dl), thus showing a positive correlation between dyslipidemia and HBA1C among patients in the population under study (Figure 4). The pattern of dyslipidemia showed that 84% of the patients with abnormal lipid profiles and 16% of patients has no lipid profile abnormality; one lipid profile abnormality was seen in 45% of the study population, 28% had two lipid profile abnormalities, and 11% of the individuals had more than two abnormal lipid profile parameters. 84% among the study group of 100 patients had lipid profile abnormalities, among these 36 patients had hypercholesterolemia, 32% had hypertriglyceridemia, 8% had high LDL-C, and 60% had

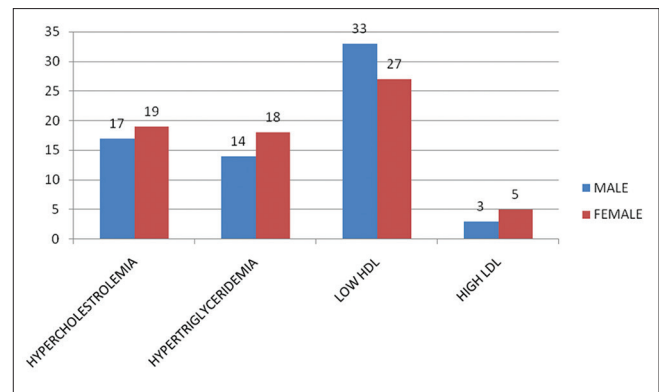


Figure 3: Lipid profile among diabetic patients

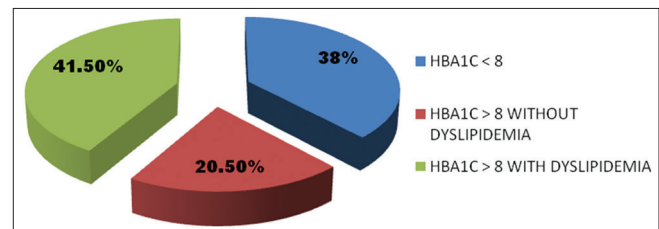


Figure 4: Correlation between glycated hemoglobin and dyslipidemia

low HDL cholesterol levels (Figure 3). Lipid abnormalities were more significant in women study patients in comparison with those of the male study patients (Figure 3). The significant correlation between HBA1C and FBG is in accordance with various previous study done all over the world. Higher levels of FBG were noted in patients with poor glycemic control (84% of total study population of Type 2 diabetics).<sup>11</sup>

## CONCLUSION

This study shows a clear and strong association between lipid profile and HBA1C. All the findings are consistent with other similar studies conducted different countries. Patients should be educated about regular monitoring of the lipid profiles and if found to be abnormal should control blood glucose and cholesterol very effectively. Achieving the target in HBA1C will contribute in improving the lipid state, and hence may lessen the diabetic complications in Type 2 diabetic patients.

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# Cytomorphological Patterns of Nodular Lesions of Liver: A 5-year Cross-sectional Study Conducted in Tertiary Care Center of Central India

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## Abstract

**Background:** The liver is one of the most common organs to undergo ultrasonographic (USG) guided fine-needle aspiration cytology (FNAC), and FNAC has become preferred modality for investigation of lesions in the liver.

**Materials and Methods:** A 5-year retrograde study on cytomorphological patterns of hepatic lesions was performed on total 341 cases. Diagnostic yield was 85.92% (293/341); almost similar results were seen in earlier studies. The main indication was single or multiple nodular lesions demonstrated clinically or by USG finding.

**Results:** The most common lesion found cytomorphologically was metastatic adenocarcinoma and constituted 41.93% (143/341), whereas hepatocellular carcinoma accounted for 17.5% (60/341) of malignant lesions of liver.

**Conclusion:** FNAC can be used as the initial modality of choice for the diagnosis of palpable nodular liver lesions as it is quick, safe, simple, and cost-effective.

**Key words:** Adenocarcinoma, Adenoma, Hepatocellular carcinoma, Fine-needle aspiration cytology

## INTRODUCTION

The liver is the second largest organ of the body. Most of the malignancies in the liver are metastatic tumors.<sup>1-3</sup> Adenocarcinoma being the most common metastatic tumors to the liver, however, hepatocellular carcinoma (HCC) is the most common primary malignant tumor in the liver.<sup>4,5</sup> Liver is the most commonly aspirated abdominal organ, i.e., about 55% of the abdominal aspirates.<sup>6</sup> Ultrasonography (USG) has been used in combination with fine-needle aspiration cytology (FNAC) in the diagnosis of liver diseases.<sup>7</sup> FNA as diagnostic modality provides accuracy with

little complications, requires minimal intervention, cheap and should be considered early in the investigative sequence.<sup>8</sup>

The differential diagnosis of hepatic mass lesions includes primary liver tumors (benign or malignant), metastatic deposits, cysts, abscesses, and granulomas. Occasionally, inflammatory lesion or diffuse liver diseases may mimic mass-like lesions.

The present study was conducted to describe the cytomorphological features in different nodular lesions of the liver.

## MATERIALS AND METHODS

The present study is a cross-sectional study conducted in the Department of Pathology, Pt. Jawaharlal Nehru Memorial Medical College (Pt. JNMHC), Raipur (Chhattisgarh, India). Pt. JNMHC is the major tertiary care center in central India. This is a retrospective study

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conducted during from June 2010 to June 2015 (5 years) and included a total of 341 patients, having nodular lesions including solitary, multiple, and diffuse as detected by clinicians and/or radiologists.

FNAC of liver lesions was conducted using the standard procedure of FNA (both guided and unguided).

Cytological smears were stained by routine hematoxylin and eosin (H and E) stain, May-Grünwald Giemsa stain and Papanicolaou stains (PAP).

Reviews of USG guided cytology slides were also done.

## RESULTS

During the period of 5 years, the total number of FNAC performed on liver, i.e., 341 cases (all USG guided) were included in the study. Out of 341 patients, 198 (58%) were male and remaining 143 (42%) were females. Male:female ratio was found to be 1.3:1. Age of the patients ranged from 1 to 80 years with mean age of 40.5 years.

Cytomorphologically, liver lesions were categorized into non-neoplastic lesion, neoplastic lesion, few suspicious cells, and inadequate for interpretation.

Regarding the FNAC diagnosis, 54 cases (15.83%) were non-neoplastic lesions, 220 cases (64.51%) were neoplastic lesions, 19 cases (5.57%) were few suspicious cells, and 48 cases (14.07%) were inadequate for opinion. Out of non-neoplastic lesions, 28 cases showed only normal hepatocytes, 20 cases were pyogenic abscess followed, and 6 cases of amoebic liver abscess.

Around 220/341 cases (64.51%) were neoplastic lesions and the majority of the cases were malignant, i.e., 217/220 cases (98%). Among the metastatic lesions, adenocarcinoma (not otherwise specified) was the most common tumor constituting 143/220 (65%) of all metastatic tumors. The most common primary malignant lesion was HCC 60/220 cases (27.27%). Three cases of each metastatic intraductal carcinoma breast, hepatoblastoma, and adenoma were reported. Two cases of each metastatic renal cell carcinoma and metastatic squamous cell carcinoma were reported. One case of each metastatic non-seminomatous germ cell tumor, metastatic gastrointestinal stromal tumor, malignant melanoma, and undifferentiated carcinoma was also reported.

The primary sites of the metastatic tumor were gallbladder, lung, colon, thyroid, breast, duodenum, cervix, stomach, and kidney (Tables 1-3).

**Table 1: Distribution of liver aspirates**

Liver aspirates	Number of cases (%)
Benign aspirates	54 (15.83)
Malignant aspirates	220 (64.51)
Suspicious of malignancy	19 (5.57)
Non-representative	48 (14.07)
Total	341 (100.00)

**Table 2: Different types of metastatic tumors**

Types	Number of cases (%)
Adenocarcinoma (NOS)	143 (65)
Breast	3 (1.36)
SCC	2 (0.90)
RCC	2 (0.90)
NSGCT	1 (0.45)
GIST	1 (0.45)
Malignant melanoma	1 (0.45)
Undifferentiated carcinoma	1 (0.45)
Total	154

NOS: Not otherwise specified, SCC: Squamous cell carcinoma, NSGCT: Non-seminomatous germ cell tumor, GIST: Gastrointestinal stromal tumor, RCC: Renal carcinoma cell

**Table 3: Incidence of various types of benign and malignant liver aspirates**

Hepatic lesions	Number of cases (%)
Benign	
Normal liver	28 (8.21)
Inflammatory	23 (6.74)
Abscess	3 (1.36)
Adenoma	3 (1.36)
Malignant	
Metastatic	154 (45.16)
HCC	60 (17.59)
Hepatoblastoma	3 (0.87)
Suspicious for malignancy	19 (5.57)
Inadequate for opinion	48 (14.07)
Total	341 (100.00)

HCC: Hepatocellular carcinoma

## DISCUSSION

Tissue diagnosis of hepatic masses is very important for early detection of lesion and management. FNAC under image guidance has gained increasing acceptance as the diagnostic procedure of choice and is very effective means of obtaining tissue from many different body sites for cytological diagnosis.<sup>9</sup> It is predominantly used for diagnosing mass lesions when there is suspicion of a neoplastic process, either primary or metastatic.<sup>4</sup> Our study emphasizes on cytomorphological patterns of different lesions which are helpful for identification of various lesions. None of the long study of this duration (5 years) with 341 cases of liver FNAC has been performed by this part of the country to best of our knowledge.

The finding of male:female (M: F) ratio in present study came to be 1.3:1, i.e., slight male predominance, whereas Nggada *et al.*<sup>10</sup> found in his study the M: F ratio to be 2.5:1 and Hao *et al.*<sup>11</sup> found that the ratio was 2.4:1.

The mean age in the present study came to be 40.5 years while the study done by Talukder *et al.*<sup>12</sup> found the mean age of diagnosing hepatic lesions to be 53 years.

The present study found 15.83 % of non-neoplastic lesion, 64.51% of neoplastic lesion, 5.57% of cases were suspicious for malignancy, and 14.07% cases were inadequate for opinion. Rasania *et al.*<sup>9</sup> in their study found 23.33% cases of non-neoplastic lesion, 67.77% of neoplastic lesion, 2.23% cases showed suspicious cell, and 6.67 cases were inadequate for opinion. Similarly, Talukder *et al.*<sup>12</sup> found 0.9% of the cases to be non-neoplastic, 93.5% cases to be neoplastic, and 6.5% cases were inadequate for opinion, whereas none of the cases were categorized under suspicious for malignancy.

In the present study, we found neoplastic lesions to be most common finding, which was similar to above studies.

We studied and evaluated the different features in different lesions as described by Ali *et al.*<sup>13</sup> and Tao *et al.*<sup>14</sup> The cytomorphological features taken in consideration included cellular arrangement, cohesiveness of cells, cell size, N/C ratio, nuclear shape and size, multinucleation, prominent nucleolus, amount of cytoplasm, vacuolation, bile pigment, and hyaline bodies.

In the present study, non-neoplastic benign lesions include pyogenic abscess and amoebic liver abscess. Many times benign hepatocellular neoplasms such as hepatic adenoma and focal nodular hyperplasia can be difficult or impossible to diagnose on FNAC alone because of their similarity with normal liver. In the present study, we found 28/341 aspirates only showing normal hepatocytes which could not be further categorized.

### Benign hepatocytes

Needle aspirates of normal liver consist predominantly of hepatocytes, with Kupffer cells and endothelial cells. The hepatocytes are present as single cells or monolayered small cell sheets or groups. These cells are round, polygonal, distinct cell border and dense granular cytoplasm. Hepatocytes frequently contain cytoplasmic pigments such as lipofuscin, hemosiderin, and bile pigments. Nucleus of hepatocytes is round/oval, with regular nuclear membrane, finely dispersed chromatin and conspicuous nucleolus. Occasionally, binucleation may be seen.

### Hepatic abscess

Aspirate from abscess shows reactive hepatocytes which showed nuclear size variation, with prominent nucleoli, but the nuclear membrane is regular with normal N/C ratio. Mitotic figure is rare. There may be the background of necrotic debris, histiocytes, and acute inflammatory cells.

## NEOPLASTIC TUMOR

- A. Metastatic tumor,
- B. HCC,
- C. Hepatoblastoma.

### Metastasis neoplasm

The liver is a common site for metastases, especially from a malignant epithelial tumor in the organs that are drained by the portal venous system, e.g., gastrointestinal tract (GIT). Other common sites are lung, breast, and kidney. Sarcomas, lymphoma, and malignant melanoma can also metastase to the liver. FNA plays very important role in diagnosis of metastatic disease along with history, clinical details, and radiological findings of the patients which could suggest a primary site. Metastatic tumors generally involve liver in form of multiple nodules of variable size.

The most common metastatic tumor is adenocarcinoma. Mainly primary tumor in GIT was found after careful search. Cytomorphological patterns of hepatic aspirate many times suggest the primary site, but in many cases, IHC and serological parameters such as alpha-fetoprotein (AFP), carcinoembryonic antigen (CEA), CA19.9, CA125-like cancer markers are required for definite diagnosis.

### Adenocarcinoma

#### Colonic adenocarcinoma

Necrotic debris often dominates the aspirate. Cells appear columnar or cuboidal. Tumor cell can be arranged in glandular or palisading pattern. Nuclei are elongated and enlarged, hyperchromatic with clumped nuclei (Figure 1a-c).

### Breast carcinoma

Usually, the patient is a known case of breast cancer. Tumor cells show the presence of intracytoplasmic lumen formation and intracytoplasmic mucin can be found (Figure 2).

### Malignant melanoma

FNA aspirate is black in appearance. Smears reveal high cellularity consisting of dispersed or loosely cohesive cluster of tumor cells. Individual cells are polygonal, may be spindled, small, or anaplastic. Nuclei appear plasmacytoid or eccentric with single prominent nucleoli.

Melanin pigment may obscure nucleocytoplasmic border and appear yellow-brown in PAP stain. Pigment might be dispersed extracellularly as well. Ocular melanomas have greater tendency to metastasize to the liver (Figure 3).

### HCC

HCC accounts for 90% of all primary cancers of the liver. Aspirates of HCC show increased cellularity and discohesiveness with crowding and overlapping of cells. The neoplastic hepatocytes are polygonal, present in thick trabecular cords greater than three cells thick. There could be solid sheets, tubular or pseudoglandular arrangement of tumor cells. The nuclei are large round with prominent nucleoli, high N/C ratio. There is moderate to severe nuclear pleomorphism and irregular nuclear membrane. Intracellular inclusions may be present. Spindle, pleomorphic, and multinucleated tumor giant cells may be present. There is also the presence of endothelial cells enclosing or transgressing the tumor cell cluster.

HCC was differentiated from other non-malignant conditions of the liver by the different features such as

cellularity, acinar pattern, trabecular pattern, hyperchromasia, uniformly prominent nucleoli, multiple nucleoli, and high N/C ratio (Figure 4 a-c).

To differentiate poorly differentiated HCC and metastatic adenocarcinoma serum level, AFP and CEA were done.

### Hepatoblastoma

Hepatoblastoma is a rare tumor in pediatric age group. It is the most common primary hepatic tumor seen under 3 years of age. Cytological smears show small, blue, and round cell tumors of childhood. Mitotic figures are frequent. The differential diagnosis includes HCC, other small round cell tumors such as neuroblastoma, rhabdomyosarcoma, Wilm tumor, and lymphoma (Figure 5a and b).

### CONCLUSION

Guided FNAC plays a key role in differential diagnosis of nodular lesions of the liver. The cytological diagnosis mainly

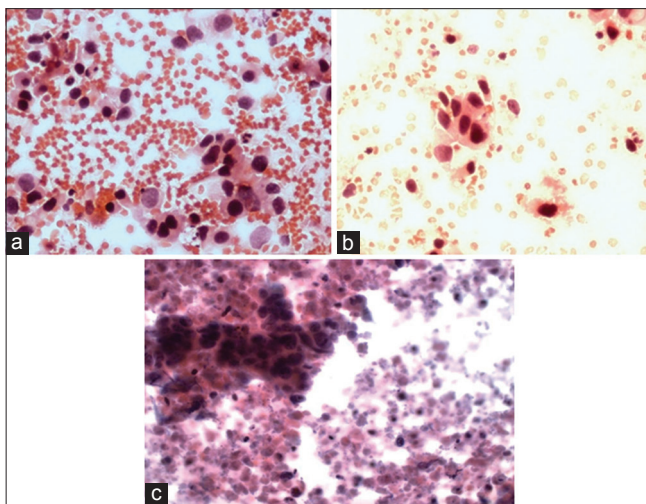


Figure 1: (a-c) Case - 59-year-old male with rectal carcinoma and secondaries in liver

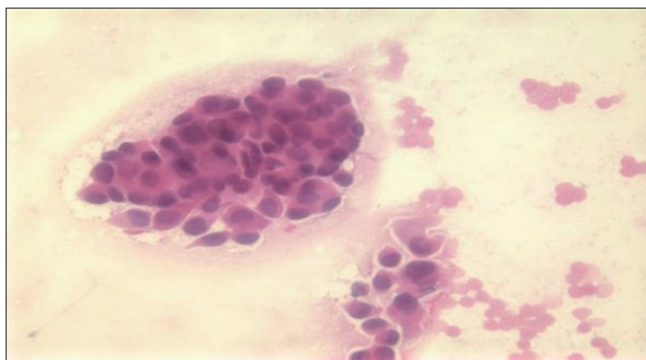


Figure 2: Case - 48-year-old female with carcinoma of breast and secondaries in liver

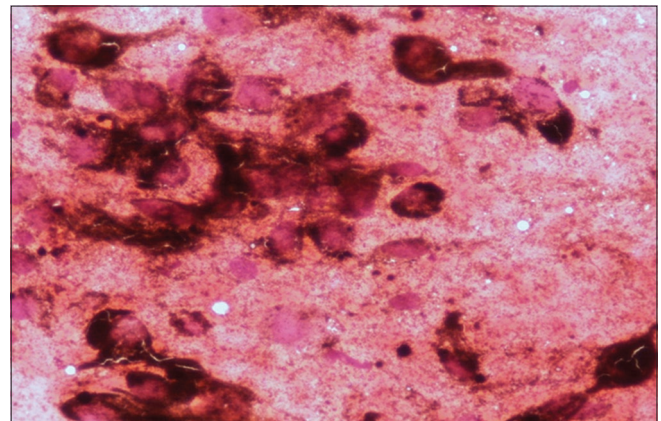


Figure 3: Case - 60-year-old male with malignant melanoma in right eye with metastasis found in liver (aspirate-black)

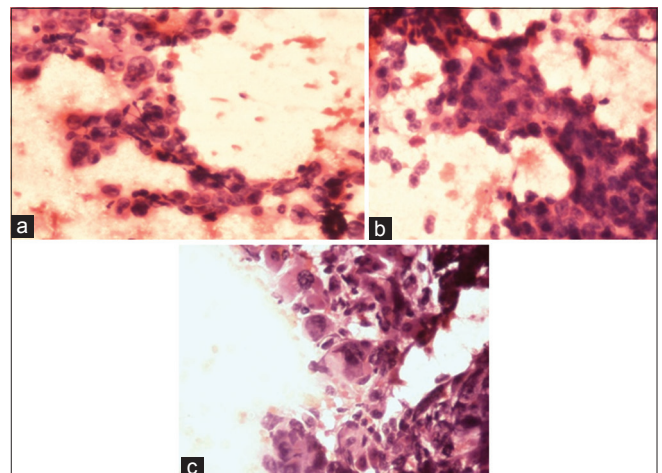
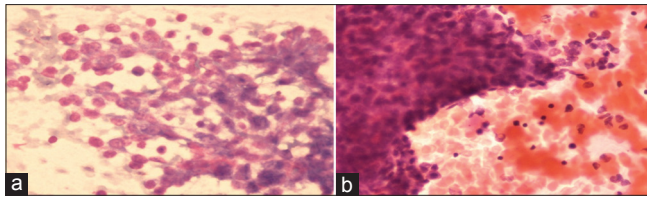


Figure 4: (a-c) Hepatocellular carcinoma



**Figure 5: (a and b) Hepatoblastoma**

depends on the recognition of distinct cytomorphological features.

The present study emphasized on recognition of unique cytomorphological patterns of distinctive liver lesions for the diagnosis by FNAC.

The present study includes a higher number of case and of long duration which would be more useful in evaluation of cytomorphological changes and in differentiation of a wide spectrum of liver masses.

## SUMMARY

FNAC can be used as the initial modality of choice for the diagnosis of palpable nodular liver lesions as it is quick, safe, simple, and cost-effective.

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# Comparing the Efficacy of Clipping versus Suture Ligation of the Cystic Duct in Laparoscopic Cholecystectomy: A Prospective Study

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## Abstract

**Introduction:** Laparoscopic cholecystectomy (LC) has been performed for decades and is a fairly standardized procedure throughout the world. Ligation of the cystic duct (CD) is popularly done with the help of metal clips (MC). There are many other techniques described in the literature to deal with ligation of the CD. Suture ligation (SL) of the duct is one such way. The technique is simple, secure, and cost-effective.

**Materials and Methods:** This is a randomized prospective study conducted in Sri Ramachandra University Hospital from January 2012 to October 2015. All patients included consented for the study. Patients who underwent subtotal cholecystectomy were excluded from the study.

**Results:** A total number of 364 patients were included in the study. In 168 patients, the CD was clipped using MC and in 196 patients, the CD was suture ligated. 31 patients had to be excluded from the study belonged to the MC group. This was based on intra-operative findings such as frozen Calot's triangle, wide CD, and Mirizzi's. Of the 196 patients in the SL group, the CD in 40 of those patients had to be divided and closed in continuity for intra-operative findings as mentioned above. The mean operating time in the MC group was 51 min 32 s and 57 min 42 s in the SL group. In the MC group, three patients had post-operative bile leak from the CD stump and two had injury to the common bile duct.

**Conclusion:** SL of the CD is a very safe and secure alternative to the application of MC. It is also very cost-effective. This technique is recommended in all laparoscopic cholecystectomies, especially in difficult cases

**Key words:** Clipping, Cystic duct, Laparoscopic cholecystectomy, Suturing

## INTRODUCTION

Laparoscopic cholecystectomy (LC) has been performed for decades and is a fairly standardized procedure throughout the world. Ligation of the cystic duct (CD) is popularly done with the help of metal clips (MC).<sup>1-4</sup> There are many other techniques described in the literature to deal with ligation of the CD. Suture ligation (SL) of the

duct is one such way. The technique is simple, secure, and cost-effective.<sup>5-7</sup>

In this study, we compare the results of two groups of patients, one in whom MC was used and the other in whom the CD was suture ligated, were studied and followed up for a period of 3-6 months.

## MATERIALS AND METHODS

This is a randomized prospective study conducted in Sri Ramachandra University Hospital from January 2012 to October 2015. All patients included consented for the study. Patients who underwent subtotal cholecystectomy were excluded from the study. The same principle of Calot's

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triangle dissection was followed for all patients and at the time of CD ligation, it was revealed to the surgeon by closed envelope method whether to clip or suture ligate the duct. All patients underwent routine ultrasound, to look for pericystic duct collection on post-operative day (POD) 7. Patients were followed up in the immediate post-operative period for complications and subsequently for long-term follow-up.

## RESULTS

A total number of 364 patients were included in the study. In 168 patients, the CD was clipped using MC and in 196 patients, the CD was suture ligated. 31 patients had to be excluded from the study belonged to the MC group. This was based on intra-operative findings such as frozen calot's triangle, wide CD, and Mirizzi's. Of the 196 patients in the SL group, the CD in 40 of those patients had to be divided and closed in continuity for intra-operative findings as mentioned above. The mean operating time in the MC group was 51 min 32 s and 57 min 42 s in the SL group. In the MC group, three patients had post-operative bile leak from the CD stump and two had injury to the common bile duct (CBD). In this Group, one patient had post-operative bile leak and one patient had post-operative biliary stricture which was an incidental finding on follow-up. 42 patients in the MC group had subclinical pericystic duct collection on POD 7 ultrasound screening. Only four patients in the SL group had a collection. However, no intervention was required for the same, and it was managed conservatively. All patients were followed up for a period of 3-6 months. No significant long-term morbidity was noted in both groups.

## DISCUSSION

LC has been the gold standard for over two decades (5). The complexity of gallbladder pathologies and its varied clinical presentation all has a bearing to what is in store for the operating surgeon. Be it a resident trainee or an expert surgeon, gallbladder surgeries always have a special reverence among all. Having been done extensively over the years, this surgery is one of the most standardized procedures today. The principle of gallbladder surgeries has been clearly defined and the techniques adapted today, all pave way for the safest possible outcome for the patient.<sup>8,9</sup>

There is clearly no discrepancy regarding the various principle outlined, but however there are various clinical scenarios that might arise during surgery that may allow the operating surgeon to do something outside the routine. Like for example, following Calot's dissection, one finds the CD to be too wide for a safe ligation using MC. By principle, the duct has to be ligated and in open surgery, the

CD is securely ligated. However, in laparoscopy through a 10 mm epigastric port, a titanium metal clip is loaded onto a 10 mm applicator, and the CD is clipped twice and divided.

In this study, we put to use the older straightforward technique of SL of the CD and see how it compares with the ever so popular application of MC. LC has been included as a part of postgraduate training in our institution. Hence, as mentioned previously, they are performed across the entire hierarchy. Having said this, it is only obvious that the operating times noted in both groups may not throw light on the "true" time taken for SL of the CD and its subsequent effect on total time taken for surgery completion as senior surgeons are surely quicker than a trainee. Another fact to be considered is difficult gallbladder surgeries, which obviously is going to take longer. In our series, the longest time duration was at 3 h 52 min 23 s. In a series of 3126 patients reported by Subhas *et al.*,<sup>1</sup> retrospectively 70 patients were identified to have an operating time of more than 3 h, the operating time ranged between 3 h and 6 h 40 min for difficult surgeries.

The biggest advantage in the current usage of MC is its quick and easy application. A cochrane review showed a statistically significant operative time difference in the SL group (9). The time taken for SL was slightly longer when compared to the application of clips (3). However, it had no bearing in terms of time taken for the surgery per say in both groups, and there was no significant time delay in the SL group. In a series of 1000 cases done with SL of CD, the mean time taken is 3.5 s.<sup>10</sup>

The cost of one pack of medium clips (6 clips) is between 550 and 750 INR, depending on various companies. Recently, the use of absorbable clips with locking has come to vogue. It is, however, more expensive as compared to routine MC. Use of endo staplers is another method to close the CD and here again, the cost of stapler and the loading gun is quite steep. In our series, we used 3-0 polyglactin, which costs between 250 and 350 INR. This single suture material, the free end was used to ligate the CD, the cystic artery and for port closure, the needle end for skin closure.

Post-operative bile leak is a serious complication following LC. While majority of surgeons prefer the use of MC in routine LC, the disadvantage is that the clip limbs may not approximate correctly or the clips might slip off the stump.<sup>6</sup> One cannot solely blame the clip, but the clip applicator might not give the adequate compression required for good approximation of the clips. Sometimes, these clips even fall off the applicator, common problem in an old applicator.<sup>7</sup> There is documented evidence of clip migration into the CBD.<sup>8</sup>

Compared to MC, it is observed that the use of absorbable locking clips shows a lesser incidence in bile leak post-operatively.<sup>2</sup> In another study similar to ours reported a similar leak rate between both groups.<sup>3</sup> However, in our series, the leak rate in the SL group was much less in comparison. On retrospective analysis, it was noted that the single case of bile leak was in a patient with a frozen Calot's triangle, and the duct had to be divided and sutured. There were no leaks in patients who had a straightforward ligation of the CD. In a series of 328 patients who underwent CD ligation with suture, only one patient had a reported bile leak.<sup>4</sup>

There is documented evidence that MC can induce inflammatory reaction around the CD stump.<sup>11</sup> To study this, we did an ultrasound screening for all patients in the study on POD and to find that, there was a radiologically significant fluid collection and fat stranding around the CD stump where MC was applied. However, this was not clinically significant as the patients had no specific symptoms.

In our cases, we used bipolar cautery for the cystic artery. Even though ElGeidie<sup>4</sup> used monopolar cautery to tackle the cystic artery with no documents thermal injury to CBD, we prefer the use of the safer option of using the bipolar cautery for precise and safe cauterization of the cystic artery.

The use of simple ligature for CD occlusion is a very safe technique to prevent post-operative bile leak.<sup>12</sup> For beginners, it might be time-consuming to do an intra-corporeal knot but in the long run, it helps to harness knowing skills very early. Furthermore, intra-corporeal knowing and suturing are very important in the practice of advanced laparoscopic procedures. In conditions where the CD is dilated and wide, the clip may not occlude the entire lumen and thus the risk of leak is high. The same when suture ligated is safe and secure.

The specimen side also needs to be ligated so as to prevent bile and stone spillage into the peritoneal cavity during surgery.<sup>4</sup>

## CONCLUSION

SL of the CD is a very safe and secure alternative to the application of MC. It is also very cost-effective. This technique is recommended in all laparoscopic cholecystectomies, especially in difficult cases.

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# Carcinoma Breast and Correlation with Estrogen and Progesterone Receptor Status in Rajendra Institute of Medical Sciences, Ranchi

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## Abstract

**Introduction:** Breast carcinoma is the second most common carcinoma in women and account for 22% of all female cancer, which is more than twice the prevalence of cancer in women at any other site. Its incidence has increased globally over the last several decades; the greatest increase has been in Asian countries. India accounts for nearly 6% of deaths and also that one in every 22 women in India are diagnosed with breast carcinoma every year. More than 80% of Indian patients are younger than 60 years of age. Hormones play an important role in the development and progression of breast cancer. Patients with hormone receptor positive tumors survive 2-3 times longer after a diagnosis of metastatic disease than do patients with hormone receptor-negative tumors.

**Purpose:** To correlate the expression of prognostic factors such as age of patient, menarche, menopause, parity, tumor size, number of lymph nodes and histological grading with estrogen, and progesterone receptor (ER/PR) status.

**Methods:** This study was carried out on a total of 75 patients with carcinoma breast admitted in the Department of General Surgery in Rajendra Institute of Medical Sciences, Ranchi from September 2012 to September 2014.

**Results:** According to the data of this study, a statistically significant correlation of ER/PR was found with menopausal status, parity, tumor size, number of lymph nodes, and tumor grade, whereas age of menarche had a significant correlation with only PR.

**Conclusion:** ER and PR status are highly important predictors in cases of carcinoma breast which necessitates routine evaluation of the hormonal receptor status for better management of the disease.

**Key words:** Carcinoma breast, Hormone receptor status, Menopausal status, Lymph node involvement, Parity, Tumor grade and size

## INTRODUCTION

Breast carcinoma is the second most common carcinoma in women and account for 22% of all female cancer, which

is more than twice the prevalence of cancer in women at any other site.<sup>1</sup> It is the most common site-specific cancer in women and is the leading cause of death from cancer for women aged 20-59 years.<sup>2</sup> It accounts for 26% of all newly diagnosed cancers in females and is responsible for 15% of the cancer-related deaths in women.<sup>3</sup> The incidence of breast cancer has increased globally over the last several decades; the greatest increase has been in Asian countries.<sup>4</sup> In Asia, breast cancer incidence peaks among women in their forties, whereas in the United States and Europe, it peaks among women in their sixties.<sup>5</sup> India accounts for nearly 6% of deaths and also that one in every 22 women

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in India are diagnosed with breast carcinoma every year with premenopausal patients constituting about 50% of all patients.<sup>6,7</sup> Over 100,000 new breast cancer patients are estimated to be diagnosed annually in India. Breast cancer cases are expected to increase by 26% by 2020, and most of these will be seen in developing countries.<sup>8</sup> Routine use of screening mammography in women >50 years of age reduces mortality from breast cancer by 33%.<sup>2</sup>

Data from the International Agency for Research on Cancer (IARC) registry suggest that 45% of newly diagnosed cases of breast cancer and 55% of breast cancer-related mortality currently occur in low- and middle-income countries. IARC trends also show a 20-30% increase in the incidence of breast cancer in developing countries during the past decade.<sup>9</sup>

More than 80% of Indian patients are younger than 60 years of age. A significant proportion of Indian breast cancer patients is younger than 35 years of age. Young age has been associated with larger tumor size, higher number of metastatic lymph nodes, poorer tumor grade, low rates of hormone receptor-positive status, earlier and more frequent locoregional recurrences, and poorer overall survival. There is a significant difference in the survival rates in developed and developing countries mainly because of a lack of early detection programs and inadequate resources for treatment.<sup>10,11</sup> Coleman reported >80% survival from breast cancer in North America and Europe compared with 60% in middle-income countries and 40% in low-income countries.<sup>12</sup>

Hormones play an important role in the development and progression of breast cancer. In postmenopausal women, hormone replacement therapy consisting of estrogen plus progesterone increases the risk of breast cancer by 26% compared to placebo. Tamoxifen, a selective estrogen receptor (ER) modulator, was the first drug shown to reduce the incidence of breast cancer in healthy women.<sup>2</sup> The best indicators of likely prognosis in breast cancer remain tumor size and lymph node status histological grade of the tumor, hormone receptor status, measures of tumor proliferation such as S-phase fraction, growth factor analysis, and oncogene or oncogene product measurements. Prognostic indices (such as the Nottingham prognostic index) have combined these factors to allow subdivision of patients into discrete prognostic groups. More recently, a computer-aided program has been developed, which incorporates the putative benefits of treatment allowing oncologist and patient to visualize the benefits of therapy.<sup>13</sup>

The patients with hormone receptor positive tumors survive two to three times longer after a diagnosis of metastatic disease than do patients with hormone receptor-negative tumors. Patients with tumors negative for both ERs and

progesterone receptors (PRs) are not considered candidates for hormonal therapy. Tumors positive for ER or PRs has a higher response rate to endocrine therapy than tumors that do not express ER or PRs. Tumors positive for both receptors has a response rate of >50%, tumors negative for both receptors have a response rate of <10%, and tumors positive for one receptor but not the other have an intermediate response rate of 33%. The determination of ER and PR status requires biochemical evaluation of fresh tumor tissue.<sup>2</sup>

Today, however, ER and PR status can be measured in archived tissue using immunohistochemical techniques. Hormone receptor status also can be measured in specimens obtained with fine-needle aspiration biopsy or core-needle biopsy, and this can help guide treatment planning. Testing for ER and PRs should be performed on all primary invasive breast cancer specimens.<sup>2</sup>

Rajendra Institution of Medical Sciences (RIMS), Ranchi gets a good number of patients with carcinoma breast and this study on carcinoma breast and correlation of prognostic factors with ER and PR status is of high clinical significance paving the path for better management of patients suffering from the dreaded disease of carcinoma breast.

## MATERIALS AND METHODS

This hospital-based study was conducted on patients with carcinoma breast admitted in the Department of General Surgery in RIMS, Ranchi from September 2012 to September 2014. A total of 75 patients with breast carcinoma were included in the study. The information such as name, registration number, age of the patient, age of menarche, age of menopause, parity of the patient, tumor size, and number of lymph nodes was collected. The specimens were sent for HPE and ER/PR status post modified radical mastectomy.

### Inclusion Criteria

All female patients with proven cases of infiltrating carcinoma of breast that were sent for histological grading and ER, PR status following surgical treatment were included in the study.

### Exclusion Criteria

Male patients:

- Patients of carcinoma breast who did not undergo surgical treatment.

## RESULTS

The mean age of the carcinoma breast patients in this study was 48.84 years with standard deviation of  $\pm 13.35$  years (Table 1).

Here, the hormone receptor positivity/negativity was compared with the age of patients. A definitive positive correlation could not be made as a number of patients as a whole was more in the age group of 35-44 years, still in the above-considered patients receptor positivity increased as the age increased. The mean age in ER+ group was  $49.36 \pm 1.94$  and  $47.8 \pm 2.55$  years in ER- group. The *P* value was 0.6364 which is statistically insignificant. In the case of the PRs, the negativity was seen maximum in age group of 35-44 years. The mean age in PR+ group was  $48.78 \pm 1.95$  and  $48.96 \pm 2.54$  years in PR- group. The *p* value was 0.9547 which makes the analysis insignificant (Table 2).

The mean age of menarche in ER+ group was  $12.26 \pm 0.13$  and  $12.12 \pm 0.18$  years in ER- group. The *P* value was 0.5443 which is insignificant. The mean age of menarche in PR+ group was  $12.39 \pm 0.136$  and  $11.88 \pm 0.16$  years in PR- group. The *P* value was 0.0254 which is significant. Hence, early menarche is associated with PR negative status (Table 3).

A total of 45 cases were premenopausal out of which ER+ as well as PR+ cases were 62.22%, whereas 30 were postmenopausal out of which ER+ was in 73.33%

**Table 1: Age distribution of carcinoma breast patients**

Age (in years)	Number of patients
25-34	5
35-44	27
45-54	16
55-64	17
65-74	6
75-84	4

**Table 2: Age and hormone receptor status is compared**

Age (in years)	ER+	ER-	PR+	PR-
25-34	4	1	4	1
35-44	17	10	17	10
45-54	9	7	9	7
55-64	12	5	12	5
65-74	6	0	5	1
75-84	2	2	4	1

ER: Estrogen receptor, PR: Progesterone receptor

**Table 3: Age of menarche and hormone receptor status**

Age of menarche	ER+	ER-	PR+	PR-
11	11	6	8	9
12	21	13	22	12
13	12	3	11	4
14	6	3	8	1

ER: Estrogen receptor, PR: Progesterone receptor

and PR+ was in 70% of cases. Hence, it was seen that postmenopausal cases had more ER as well as PR positivity (Table 4).

As the parity has increased, the ER as well as PR positivity has increased. The mean parity in the ER+ group was  $3.3 \pm 0.17$  whereas it was  $2.2 \pm 0.3$  in the ER- group. The *P* value is 0.0012 and it was significant. The mean parity of PR+ group was  $3.4 \pm 0.17$ , whereas it was  $2.038 \pm 0.28$  in the PR- group. The *P* value was  $<0.0001$  and it was highly significant (Table 5).

In this study, the most tumors were of size 2-3 cm and as the size of the tumor increased, the hormone receptors negativity has increased. The mean tumor size in ER+ group was  $2.61 \pm 0.13$  and  $4.34 \pm 0.26$  cm in ER- group. The *P* value was  $<0.0001$  which makes the result highly significant. The mean tumor size in PR+ group was  $2.6 \pm 0.13$  and  $4.115 \pm 0.28$  cm in PR- group. The *P* value was  $<0.0001$  which is highly significant (Table 6).

In most of the cases, the lymph nodes number was between 0 and 2, and they were mostly hormone receptor positive. The mean number of lymph nodes was  $0.82 \pm 0.12$  in the ER+ group while it was  $4.24 \pm 0.59$  in the ER- group. The *P* value was  $<0.0001$  which is highly significant. The mean number of lymph nodes was  $0.857 \pm 0.146$  in the PR+ group and was  $4.038 \pm 0.577$  in

**Table 4: Menopausal status and hormone receptor status**

Menopausal status	ER+	ER-	PR+	PR-
Pre-menopausal	28	17	28	17
Post-menopausal	22	8	21	9

ER: Estrogen receptor, PR: Progesterone receptor

**Table 5: Parity and hormone receptor status**

Parity	ER+	ER-	PR+	PR-
0	1	4	1	4
1	1	5	1	5
2	11	5	7	9
3	15	6	17	4
4	16	3	17	2
5	3	2	3	2
6	3	0	3	0

ER: Estrogen receptor, PR: Progesterone receptor

**Table 6: Tumor size and hormone receptor status**

Tumor size	ER+	ER-	PR+	PR-
<2	6	0	6	0
2-3	37	7	34	10
>3-5	6	10	8	8
>5	1	8	1	8

ER: Estrogen receptor, PR: Progesterone receptor

the PR– group. The  $P$  value was  $<0.0001$  which is highly significant (Table 7).

In this study, most of the cases were of Grade I and they showed hormone receptor positivity, and the negativity was found to increase with an increase in grade of the tumor. In Grade I, II and III tumors the ER positive cases were 84.21%, 78.26% and 0%, respectively. The  $p$  value is  $<0.0001$  which makes the association between grade and ER highly significant. The Grade I, II and III tumors showed PR positivity of 89.47%, 60.87% and 7.14%, respectively. The  $P$  value is  $<0.0001$  which is highly significant too (Table 8).

## DISCUSSION

Carcinoma breast has known risk factors each of which was correlated separately with ER and PR status.

### Age and Hormone Receptor Status

Fisher *et al.*, in 1980, studied 178 invasive breast cancer cases. Well-differentiated tumors were more frequently ER+ in older women.<sup>14</sup>

Mohammed *et al.*, in 1986, reviewed 490 consecutive human breast biopsy and mastectomy specimens which were correlated with ER and PR content of the tissue. 63% of the patients with Grade IV infiltrating ductal carcinoma were younger than 53 years of age ( $P < 0.001$ ). Patients younger than 53 years of age with Grade II and III infiltrating ductal carcinoma also had significantly lower levels of ERs, but not of PRs, than those patients older than 53 years of age ( $P < 0.001$ ).<sup>15</sup>

Ruder *et al.*, in 1989, reported a study over 171 Israeli women diagnosed with breast cancer and found that age tended to be associated positively with both ER+ and PR+.<sup>16</sup>

**Table 7: Lymph node number and hormone receptor status**

Lymph node number	ER+	ER–	PR+	PR–
<2	37	5	36	6
2-5	13	11	13	11
>5	0	9	0	9

ER: Estrogen receptor, PR: Progesterone receptor

**Table 8: Histological grade and hormone receptor status**

Histological grade	ER+	ER–	PR+	PR–
I	32	6	34	4
II	18	5	14	9
III	0	14	1	13

ER: Estrogen receptor, PR: Progesterone receptor

Amaral and Sergio, in 2001, studied 306 patients with infiltrating ductal carcinoma and found that both ER and PR were significantly associated ( $P < 0.05$ ) with patient's age ( $<60$  years vs.  $>60$  years). When the association was studied between different levels of positivity for HR (+++ vs. ++ vs. + vs. negative) and patient's age ( $<60$  years vs.  $>60$  years), significant  $P$  value ( $P < 0.01$ ), for both ER and PR was found.<sup>17</sup>

Britton *et al.*, in 2002, studied 1556 women aged 20-44 years with carcinoma breast. As age increased, the proportion of women with ER+PR+ tumors increased, and this finding corresponded primarily with a decline in the proportion of women diagnosed as having ER– PR– tumors.<sup>18</sup>

Alvarez Goyanes *et al.*, in 2008, examined 1509 tumors from Cuban women diagnosed with breast cancer. Analysis of age at the time of diagnosis showed that ER expression was greater in patients in the group aged  $>50$  years ( $P < 0.05$ ).<sup>19</sup>

Pourzand *et al.*, in 2011, organized an analytic cross-sectional study of 105 women diagnosed with breast cancer and found a direct correlation between positive PR status and being younger than 40 ( $P < 0.05$ ). Also, compared with older women, young women had tumors that were more likely to be large in size and have higher stages ( $P < 0.05$ ).<sup>20</sup>

Ahmed *et al.*, in 2011, studied 157 formalin-fixed, paraffin embedded tissue block samples from the breast lesions. Primary breast cancer cases had their ages ranging from 21 to 80 years with a mean age of 46 years.<sup>21</sup>

In this study (Tables 1-3), out of 75 cases of carcinoma breast, who were from 25 to 84 years of age (mean age  $48.84 \pm 13.35$ ), ER+ and PR+ cases were 50 (66.66%) and 49 (65.33%), respectively. The mean age in ER+ group was 49.36 and 47.8 in ER– group. The  $P$  value was statistically insignificant. The mean age in PR+ group was 48.78 and 48.9 in PR– group. The  $P$  value was insignificant. Still, as the age increased, ER and PR positivity increased which is in accordance with the above studies.

### Age of Menarche and Hormonal Receptors

Rosen found the association between ER– and early menarche statistically borderline ( $P = 0.09$ ).<sup>22</sup>

Amaral and Sergio, in 2001, found a statistically significant association between PR– and early menarche ( $<11$  years) ( $P < 0.05$ ).<sup>17</sup>

In this study, the mean age of menarche in ER+ group was 12.26 and 12.12 years in ER-group ( $P = 0.5443$ , insignificant), whereas it was 12.39 years in PR+ group and

11.88 years in PR– group ( $P = 0.0254$ ) which is significant. This finding is in accordance with the above findings.

### Menopausal Status and Hormonal Receptors

Mohla *et al.*, in 1982, studied 146 black women with breast cancer and found that postmenopausal patients and primary tumors showed higher ER+ than premenopausal patients and metastatic sites, respectively.<sup>23</sup>

Ruder *et al.*, in 1989, found that being postmenopausal, older at menopause or at first birth, were correlated positively with ER and negatively with PR.<sup>16</sup>

Amaral and Sergio, in 2001, found a statistically significant positive association between ER and menopausal status (pre- vs. post-menopause,  $P = 0.0008$ ). The association observed between PR and this same variable was small and not statistically significant ( $P = 0.37$ ).<sup>17</sup>

In this study, postmenopausal cases had more ER and PR receptor positivity similar to the findings as that of Mohla and Eisenberg but, not as that of Ruder, who found a negative correlation of PR with menopausal status.

### Parity and Hormonal Receptors

Ruder *et al.* found that nulliparity was correlated positively with ER and negatively with PR.<sup>16</sup>

Britton *et al.* found that nulliparous women were at increased risk of all tumor types except ER– PR+. An inverse association was observed between months of lactation and each of the hormone receptor tumor subtypes, with the strongest risk reduction observed for ER+ PR– tumors.<sup>18</sup>

In this study, as the parity has increased, the ER and PR positivity has increased similar to above studies.

### Tumor Size and Hormonal Receptors

Amaral and Sergio found statistically significant association between ER and PR+ tumors and tumor size  $<4.0$  cm ( $P < 0.005$ ).<sup>17</sup>

Alvarez Goyanes *et al.* found that ER expression was associated with low nuclear grade and histological grade, and with smaller tumor size ( $P < 0.05$ ).<sup>19</sup>

Pourzand *et al.* found that younger women had tumors that were more likely to have higher stage, larger size, and PR+ ( $P < 0.005$ ).<sup>20</sup>

In this study, as the size of the tumor increased, the ER and PR– has increased which was statistically significant ( $P < 0.0001$ ) and is in accordance with the above studies.

### Lymph Node Number and Hormonal Receptors

Stierer *et al.* and MacGrogan *et al.* showed that the presence of hormonal receptors (ER and PR) were not associated with nodal status.<sup>24,25</sup>

Amaral and Sergio did not find any association of nodal status with hormonal receptors.<sup>17</sup>

Alvarez Goyanes *et al.* found that ER expression tended to decrease as the number of metastatic axillary lymph nodes increased, although this association was not statistically significant.<sup>19</sup>

Ahmed *et al.* found a significant positive association between ER or PR expression with lymph node involvement ( $P = 0.004$  and  $P = 0.022$ , respectively).<sup>21</sup>

Pourzand *et al.* found that 59.6% of ER+ patients had lymph node involvement; 60.4% of ER– patients had involved nodes, and the difference was not statistically significant ( $P = 0.88$ ). Similarly, 57.1% of PR positive patients had lymph node involvement compared with 64.2% of PR negative patients and it was also not statistically significant ( $P = 0.42$ ).<sup>20</sup>

In this study, a significant association of lymph node status and ER/PR receptors was found. This finding is in accordance with that of Ahmed *et al.*

### Histological Grade and Hormone Receptor Status

Fisher *et al.* (1980) found positive ER to be significantly associated with high nuclear and low histologic grades.<sup>14</sup>

Mohla *et al.* also found a significant correlation between the ER+ and tumor grade.<sup>23</sup>

Mohammed *et al.* studied the ER and PRs in human breast cancer and correlation with histologic subtype and degree of differentiation. Of the four grades of differentiation, the less differentiated Grade III and IV tumors showed significantly lower levels of ER and PRs in infiltrating ductal and lobular carcinoma ( $P < 0.001$ ). Patients younger than 53 years of age with Grade II and III infiltrating ductal carcinoma also had significantly lower levels of ERs, but not of PRs, than those patients older than 53 years of age ( $P < 0.001$ ).<sup>15</sup>

Amaral and Sergio found statistically significant association between ER and PR+ tumor and low histological grade ( $P = 0.01$ ).<sup>17</sup>

Alvarez Goyanes *et al.* also found significant association between ER and PR+ tumors and low histological grade ( $P = 0.01$ ).<sup>19</sup>

Ahmed *et al.* found no statistically significant association between ER, PR and tumor grade.<sup>21</sup>

In this study, the Grade I, II and III tumors showed ER positivity of 84.21%, 78.26% and 0%, respectively, and PR+ of 89.47%, 60.87% and 7.14%, respectively, which is highly significant statistically ( $P < 0.0001$ ) and is in accordance with the above studies.

## CONCLUSION

This study conducted at RIMS, Ranchi evaluated the ER/PR status and correlation with other prognostic factors.

According to the data of this study, a statistically significant correlation of ER/PR was found with menopausal status, parity, tumor size, number of lymph nodes and tumor grade, whereas age of menarche had significant correlation with only PR.

To conclude, ER/PR status is highly important predictor in cases of carcinoma breast which necessitates routine evaluation of the hormonal receptor status for better management of the disease.

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# Functional Outcome of Hahn-Steinthal Fracture Capitellum Fixed with Kirschner-wires Via Posterolateral Approach

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## Abstract

**Introduction:** Isolated coronal shear fractures of the capitellum are extremely rare injuries. Authors continue to differ about the preferred methods of treatment and its results on the functional outcome. If the anatomical reduction is not achieved, elbow function is sub-optimal.

**Materials and Methods:** A retrospective evaluation of 15 patients, 11 females and 4 males, with Type 1/Hahn-Steinthal fracture capitellum according to Bryan-Morrey classification system, within the age-group (21-50), operated between February 2002 and August 2014 with open reduction and internal fixation in all cases with multiple (2-4) Kirschner-wires (K-wires), (3 K-wires in 11 patients, 2 K-wires in 2 patients, and 4 K-wires in 2 patients) in a Crisscross manner through a minimally invasive posterolateral approach. All 15 patients were available for clinical and radiographic evaluation at a minimum follow-up of 2-year postoperatively. The evaluation of functional outcome was done clinically, radiographically and accessed through Mayo elbow performance index, and the American shoulder and elbow surgeons (ASES) scale.

**Results:** All the 15 fractures united uneventfully by the 6-month follow-up on an average. The average Mayo score was 99, i.e., excellent in all 15 cases. The average ASES score was 91. Range of motion (ROM) in flexion/extension averaged 154°, while ROM in supination/pronation averaged 89°. All fractures healed in anatomic position with, no arthritis, avascular necrosis or heterotopic ossification was observed.

**Conclusion:** The authors hereby recommend multiple (2-4) K-wires as an effective modality of choice in Type-1 capitellum fractures inserted via a minimally invasive posterolateral approach, hence facilitating early mobilization, to achieve excellent functional outcomes.

**Key words:** Capitellum, Functional outcome, Hahn-Steinthal fracture, Kirschner-wires, Posterolateral approach

## INTRODUCTION

Fracture of the capitellum of the humerus was first reported in 1853 by Hahn of Germany since then fracture of the capitellum has been an extremely rare injury accounting for 0.5-1% of the elbow fractures and 6% of the distal humerus fractures.<sup>1</sup> These fractures are frequently missed on the first examination, which also

contributes to the rarity of these fractures because they are not obvious on anteroposterior (AP) radiographs as the fracture line may not be recognized against the background of the distal humerus. Whereas they are best seen on a true lateral view.<sup>2</sup> Bryan and Morrey classification modified by McKee, classifies capitellar fractures as Type 1-3 and Type 4.<sup>3,4</sup> Type 1, often referred to as the Hahn-Steinthal fracture, is a shear fracture in the coronal plane involving most of the capitellum and little or none of the trochlea (Figure 1). Many treatments have been advocated for these injuries including closed reduction (Dushuttle *et al.*, 1985; Ochner *et al.* 1996), open reduction and internal fixation (Ring *et al.*, 2003; Dubberly *et al.*, 2006; Ruchelsman *et al.*, 2008), excision of the fracture fragments (Collert, 1977; Grantham *et al.*, 1981), prosthetic replacement (Jakobsson, 1957; Cobb and

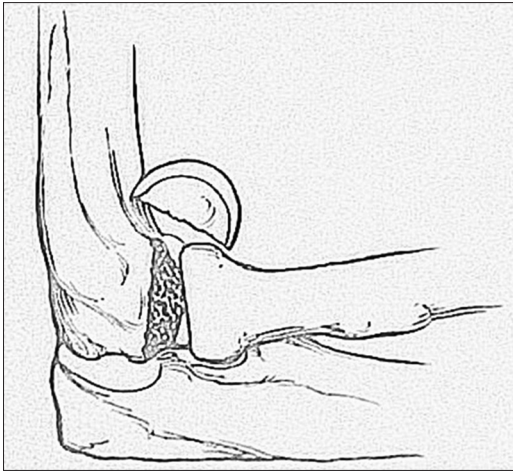
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**Figure 1: Hahn-Steinthal/Type-1 capitellum fracture**

Morrey 1997), and fixation or excision of the fragments under arthroscopy (Hardy *et al.*, 2002).

Closed reduction of Type I capitellar fractures has been reported in a few series.<sup>5,6</sup> Disadvantages of this treatment are the long period of immobilization and unsatisfactory functional results.<sup>4,7</sup> Fitz-gerald says: "In all cases, the fragments should be removed as soon as possible after the injury."<sup>8</sup> But after resection of the capitellar fragment, the remaining raw bone surface predisposes the elbow to capsular adhesions and results in restricted elbow mobility, instability, valgus deformity of the elbow, and risk of subsequent ulnar neuritis.<sup>2</sup> Lee *et al.* favor the employment of a bone peg or steel pin, while Buxton *et al.* sutures through drill holes or uses a transversely inserted bone peg, running into the trochlea. Immobilization to prevent tearing of the delicate new capillaries with their trailing osteoblasts explains this attitude for mechanical fixation. Various methods of mechanical fixation have been proposed such as Kirschner-wires (K-wires), cortical/malleolar screws, lag screws, absorbable screws, and herbert screws. However, yet there is no universal consensus on the preferred modality of fixation for these fractures. Internal fixation with K-wire has been the historically preferable method of fixation, as the cartilaginous component of the fragment is often very large with a minimal amount of cancellous or subchondral bone.<sup>9-11</sup> However, some studies suggest that K-wires penetrate the articular surface do not provide stable fixation and cast immobilization is mandatory for a long period. K-wires do not offer compression at the fracture site and require subsequent removal.<sup>2</sup>

In this study, we have tried to demonstrate how K-wires can be used in Type 1 capitellum fractures without damaging the articular cartilage, providing a rigid jigsaw puzzle like reduction with adequate compression, with early immobilisation, with no need for removal and as a

cost-effective method, with excellent results achieved in terms of clinical, radiographic, and functional outcomes (assessed via Mayo elbow score and American shoulder and elbow surgeons [ASES] index).

## MATERIALS AND METHODS

Between February 2002 and August 2014, 15 patients who have sustained isolated coronal shear capitellum fracture presented to our hospital (Table 1). They were diagnosed and treated operatively within 2 weeks after injury (range 0-14 days), with a mean of 6 days. They were eleven females and four males; their age ranged from 21 to 50 years with 5 patients younger than 30 years. The right arm was dominant in all 15 patients, whereas the injured arm being left in 11 patients and right in 4 patients (Table 1). The fracture type was determined by a lateral radiograph, which showed a characteristic semilunar fragment detached from the humeral condyle and lying supero-anteriorly to the distal humerus, suggesting a completely displaced fracture of capitellum, a typical Hahn-Steinthal/Type 1 fracture, according to Bryan-Morrey classification system. An AP radiograph did not reveal a definite fracture (Figures 2 and 3). No other associated injuries were detected. Computed tomography-scan was not done in any of the cases due to financial constraints. All 15 patients were available for clinical and radiographic evaluation at a minimum follow-up of 2-year postoperatively.

We underwent open reduction and internal fixation in all cases with multiple (2-4), (3 K-wires in 11 patients, 2 K-wires in 2 patients, and 4 K-wires in 2 patients) K-wires in a criss-cross manner via a minimally invasive posterolateral approach.

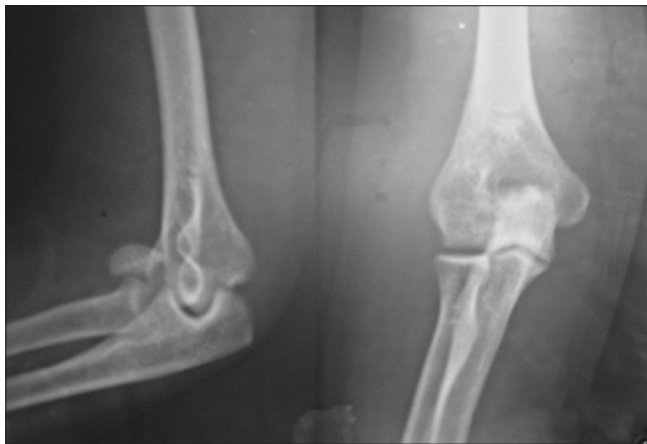
### Surgical Technique

We took a gentle curved incision beginning over the posterior surface of the lateral humeral epicondyle, 5 cm proximal to the elbow joint, and then continuing downward up to the radial head posteriorly, taking due care that the incision should not extend beyond the annular ligament to avoid injury to the posterior interosseous nerve. And also fully pronating the forearm to move the posterior interosseous nerve away from the operative field. Incising the deep fascia in line with skin incision, the lateral humeral condyle was exposed by elevating the triceps from it, taking due care to preserve the lateral ulnar collateral ligament origin at the lateral epicondyle. Further retracting the triceps posteriorly and brachioradialis anteriorly, the dissection is continued distally identifying the interval between extensor carpi ulnaris and anconeus (Kocher's interval), after which capsulotomy is done by incising the capsule anteriorly over the capitellum. Subperiosteal reflection of brachioradialis, extensor carpi

**Table 1: Patient demographics**

S. No.	Gender	Age	Dominant	Injured	Mechanism	Type	Follow-up months	Management
1	Female	21	Right	Left	On extended elbow	1	28	ORIF with 3 K-wires
2	Female	36	Right	Right	On extended elbow	1	24	ORIF with 2 K-wires
3	Female	27	Right	Left	On extended elbow	1	36	ORIF with 3 K-wires
4	Male	35	Right	Left	On extended elbow	1	48	ORIF with 3 K-wires
5	Male	38	Right	Left	On extended elbow	1	35	ORIF with 3 K-wires
6	Female	42	Right	Right	On extended elbow	1	29	ORIF with 3 K-wires
7	Male	50	Right	Left	On extended elbow	1	32	ORIF with 3 K-wires
8	Male	41	Right	Left	On extended elbow	1	24	ORIF with 3 K-wires
9	Female	31	Right	Right	On extended elbow	1	28	ORIF with 3 K-wires
10	Female	46	Right	Left	On extended elbow	1	36	ORIF with 4 K-wires
11	Female	39	Right	Left	On extended elbow	1	18	ORIF with 3 K-wires
12	Female	50	Right	Left	On extended elbow	1	36	ORIF with 3 K-wires
13	Female	27	Right	Left	On extended elbow	1	48	ORIF with 3 K-wires
14	Female	22	Right	Right	On extended elbow	1	40	ORIF with 4 K-wires
15	Female	30	Right	Left	On extended elbow	1	30	ORIF with 2 K-wires
Average	73% Females	35 years					32 months	

K-wires: Kirschner-wires

**Figure 2: Pre-operative X-ray****Figure 3: Post-operative X-ray**

radialis anteriorly and triceps posteriorly will improve joint exposure and make space for K-wire insertion from the posterior aspect. Further manipulation of the fragment by simply pressing it into the joint space, allowed a Jigsaw puzzle

like reduction, which was held in correct position by all the natural forces in that region like the cup-like head of the radius, the humerus, the lateral ligaments, and the ulna, which was further consolidated by inserting multiple (2-4) K-wires from posterior to anterior direction in a criss-cross manner to give rotational stability, at the same time avoiding any penetration of the articular cartilage (Figures 4 and 5). The K-wires were buried into the posterior aspect of the humerus to avoid any impingement. The radial wrist extensors and the triceps are repaired to the soft-tissue cuff on the lateral supracondylar ridge, and the Kocher interval is closed in continuity with the proximal exposure of the lateral column to preserve the precarious blood supply of the capitellum. An intraoperative dynamic examination showed satisfactory stability of the osteosynthesis and anatomic articular congruity. Postoperatively all the patients were immobilised in an above elbow slab at 90° flexion, with forearm in supine position for 3 weeks. At first follow-up after 3 weeks, slab was removed and aggressive physiotherapy was started. At subsequent follow ups clinical examination for evaluation of ROM including the arc of flexion-extension measured by handheld goniometer, and stability evaluated by history and provocative physical examination manoeuvre for valgus and varus. Serial AP and lateral radiography were done for fracture union, osteonecrosis, heterotopic ossification (HO), or osteoarthritis.

Functional evaluation at the last visit was done with the use of [A] ASES assessment form,<sup>12</sup> [B] the Mayo elbow performance index (MEPI) which is based on 100 points scale.<sup>13</sup>

## RESULTS

All the 15 fractures united uneventfully by the 6-month follow-up on an average. The average Mayo score was 99,

i.e., excellent in all 15 cases. The average ASES score was 91. Range of motion (ROM) in flexion/extension averaged 0-154° (Figures 6-9), while ROM in supination/pronation averaged 89° (Table 2).

Radiographically, there were no complications seen such as arthritis, avascular necrosis, or heterotopic ossification. There were also no instances of instability, nonunion, hardware failure, or iatrogenic fracture on



Figure 4: Post-operative X-ray



Figure 7: Range of extension

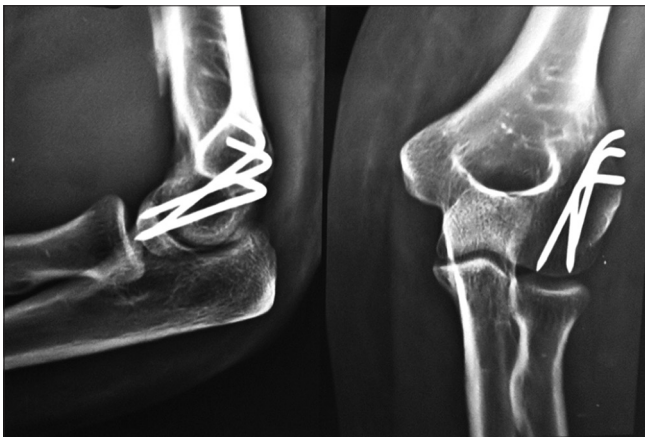


Figure 5: Post-operative X-ray



Figure 8: Range of flexion



Figure 6: Range of flexion



Figure 9: Range of extension

**Table 2: Clinical outcomes**

S. No.	Mayo score	Total ASES index	ROM-flex/ext	ROM-sup/pron	Complication
1	100	97	0-160	90-90	None
2	100	90	0-155	90-90	None
3	100	89	0-145	90-90	None
4	100	90	0-152	90-90	None
5	100	98	0-160	90-90	None
6	100	86	0-145	90-80	None
7	100	90	0-155	90-90	None
8	100	94	0-160	90-90	None
9	100	92	0-160	90-90	None
10	85	82	0-140	80-80	Mild pain
11	100	88	0-150	90-90	None
12	100	91	0-160	90-90	None
13	100	93	0-156	90-90	None
14	100	95	0-160	90-90	None
15	100	90	0-160	90-90	None
Average	99	91	0-154.5	89.33-88.66	

ASES: American shoulder and elbow surgeons, ROM: Range of motion

the most recent radiographs (Table 3). All patients were satisfied with the outcome and returned to their pre-injury status resuming all daily routine activities, except one who was concerned about the mild pain at his last follow-up.

## DISCUSSION

Presently, the preferred method of treatment for capitellum fractures is open reduction and internal fixation, and a wide variety of techniques are described such as K-wires, compression screws, Herbert screws, and biodegradable pins.

Cannulated screw fixation enables adequate interfragmentary reduction and compression. Contrary to pin or wire techniques, this type of fixation does not require further hospital admissions and the rehabilitation program starts earlier and is uninterrupted.<sup>14,15</sup>

Cannulated screws introduced posteriorly through the humerus into the capitellum avoid this problem.<sup>16</sup> However, if the osteochondral fragment is small, the screw may split it. Headless double-threaded screws (Herbert type) could also be used.<sup>14,10</sup> However, we feel that for thin fragments this type of screw can fail to confer satisfactory fixation due to its compression mechanism. Headless screws such as Herbert screw and biodegradable screws can be used without the need for removal; however, these are substantially expensive and special instruments and experience are needed when compared with standard convenient screws. Poynton *et al.*, in his study, divided patients into two groups consisting of K-wire fixation and Herbert screw fixation, and then, reported better results in the screw group.<sup>14</sup>

**Table 3: Radiographic outcomes**

S. No.	Arthritis	Non-union	HO	AVN	Instability	Union
1	Grade 0	No	None	Absent	None	Yes
2	Grade 0	No	None	Absent	None	Yes
3	Grade 0	No	None	Absent	None	Yes
4	Grade 0	No	None	Absent	None	Yes
5	Grade 0	No	None	Absent	None	Yes
6	Grade 0	No	None	Absent	None	Yes
7	Grade 0	No	None	Absent	None	Yes
8	Grade 0	No	None	Absent	None	Yes
9	Grade 0	No	None	Absent	None	Yes
10	Grade 0	No	None	Absent	None	Yes
11	Grade 0	No	None	Absent	None	Yes
12	Grade 0	No	None	Absent	None	Yes
13	Grade 0	No	None	Absent	None	Yes
14	Grade 0	No	None	Absent	None	Yes
15	Grade 0	No	None	Absent	None	Yes

AVN: Avascular necrosis, HO: Heterotopic ossification

However, we feel that each mode of treatment has its proponents and opponents. In this cohort analysis and evaluation, a minimally invasive posterolateral approach was used which did not necessitate extensive soft tissues dissection to avoid postoperative scarring, HO and hence preserving the precarious blood supply of the capitellum. The exposure is merely to achieve an anatomic jigsaw-puzzle like reduction and visualize the passage of the K-wire through the elbow joint. Stable fixation could be achieved by this method as MEPI scores, and ASES index showed the results which far exceeded the results of Ruchelsman *et al.*<sup>17</sup> who followed extensile lateral approach with elevation of common extensor and pronator tendons to insert headless screws from anterior to posterior direction. The overall ROM results and the elbow specific outcome compared favorably with Doornberg *et al.*<sup>18</sup> and by far exceeded the results of Stamatis and Paxinos.<sup>19</sup> The mean UHM arc of 0-154°, a mean MEPI score of 100 points corresponded with a series of 17 patients

by Dubberley *et al.*,<sup>20</sup> who used cancellous lag screws inserted from posterior to anterior direction with flexion contracture in his series (40°-22°). The significant loss of terminal extension in other studies is due to the extended operative dissection (Ruchelsman *et al.*<sup>17</sup>) to create a space for AP insertion of screws while K-wire does not necessitate that extent of dissection.

The number of 15 patients reported in this cohort is regarded a considerable size, compared to a series of Ring *et al.*<sup>21</sup> MacDermid *et al.*<sup>22</sup> Mighell *et al.*<sup>23</sup> However, we as authors understand the limitation of our study, which being restricted to only Type-1 capitellum fractures. Furthermore, the average follow-up in this series was 32 months. While it is clear that complications such as pain and instability show up early, longer follow-up is essential to assess the development of post-traumatic arthritis. Hence, we recommend that a more extensive study involving all types and with a longer follow-up period needs to be done.

## CONCLUSION

In Hahn-Steinthal (Type-1) fracture capitellum, the fixation method used should depend on the fracture type, anatomic articular reduction, minimal articular damage, minimal soft tissue damage, rigid fixation, early immobilization, and cost-effectiveness of the implant.

We through our study recommend using multiple K-wires (2-4) inserted in a criss-cross manner through a minimally invasive posterolateral approach which helps in achieving an anatomic jigsaw-puzzle like reduction without any extensive dissection hence preserving the precarious blood supply of the capitellum and also allowing early mobilisation to achieve the excellent functional results assessed via Mayo score and ASES index.

Although our series is one of the largest series in the literature, we believe larger series that includes other types of capitellum fractures as well, with a longer follow-up and with control groups are necessary to draw more firm conclusions.

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# Prevalence of Ophthalmic Disorders in Hearing Impaired School Children

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## Abstract

**Introduction:** Vision forms the major aspect in understanding the surroundings and to communicate with others in a hearing impaired child and so even a mild refractive error will lead to significant handicap in the quality of life for the child and retards the overall development.

**Aim:** To know the causes and to study the prevalence of ophthalmic disorders in hearing impaired school children.

**Materials and Methods:** A cross-sectional study of 350 children was conducted in a special school for deaf. Approval by the Institutional Ethical Committee and permission of appropriate authorities were obtained. All children from class 1 to 10 of both genders were screened. Those not willing to participate, not cooperative, who were not available at the time of examination were excluded in the study. Demographic data, history from every child was recorded with the help of teachers in the school. Complete ophthalmological examination with refraction and systemic examination was done.

**Results:** Of the 359 children examined, males were 211 and females comprised 148. Among these, 104 were found to have one or more ophthalmic abnormalities. Thus, the prevalence of ophthalmic disorders is 29% in this study. Refractive errors predominated in our study with the prevalence of 16.99% (61/359), followed by Vitamin A deficiency, heterochromia iridis, pigmentary retinopathy, and retinitis pigmentosa. More than 70% of ophthalmic abnormalities are either preventable or treatable in our study.

**Conclusion:** The prevalence of ophthalmic disorders in hearing impaired schools is more compared to normal schools. Visual impairment in these children can be prevented by regular eye screening by an ophthalmologist and early recognition and treatment of the disorder.

**Key words:** Heterochromia iridis, Ophthalmic disorders, Pigmentary retinopathy, Refractive errors, Retinitis pigmentosa

## INTRODUCTION

Hearing impairment in children leads to significant appreciation of other senses such as vision, smell, and touch. Vision forms the major aspect in understanding the surroundings and to communicate with fellow beings. When one of these is seriously impaired, the others are used to compensate the disability, so the hearing impaired

population may compensate by making greater use of visual-perceptual cues than their normal hearing peers, and thus, even a mild refractive error may reduce the visual cues available to the hearing impaired person.<sup>1</sup> It also leads to severe impairment in the mental condition of the child and retards the overall development. Hence, it is essential to detect, diagnose, and treat the possible ophthalmic conditions for a better living of a hearing impaired child. If both hearing and speech are affected, these children also develop mental retardation the World Health Organisation estimates the prevalence of mental retardation in the general population (across all ages) to be 2%, being 3% in individuals below the age of 18 years.<sup>2</sup> Despite the magnitude of the problem, affected individuals are underserved due to a lack of awareness about their problems, even among health-care providers.

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## Aim

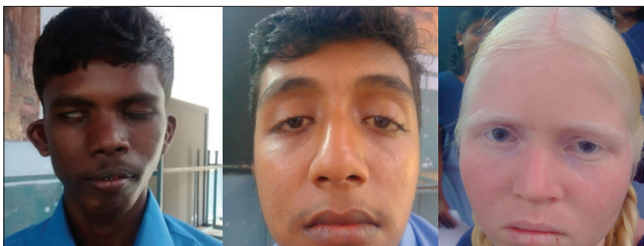
To know the causes and to study, the prevalence of ophthalmic disorders in hearing impaired school children.

## MATERIALS AND METHODS

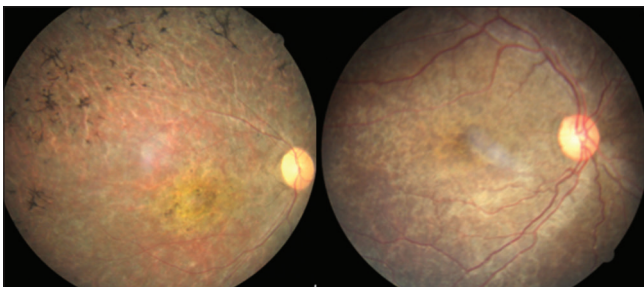
This cross-sectional study was conducted in a special school in Tirunelveli, Tamil Nadu. To have 95% confidence interval, we planned to enroll 359 hearing impaired children into this study. The Institutional Ethics Committee approval and authorities' permission to conduct the study in the special school were obtained. All children from class 1 to 12 of both genders were included in the study. Those not willing to participate, not cooperative, who were not available at the time of examination were excluded. Demographic data, history from every child, with the help of teacher was noted. The ophthalmologic workup included visual acuity assessment, pupillary evaluation, ocular motility examination, and alternate cover test and fundus examination. Snellen's chart was used for examining children. A cycloplegic refraction was done where indicated. Systemic examination was also carried out.



**Figure 1: Heterochromia iridis - total, partial, and a child with bilateral congenital ptosis**



**Figure 2: Right congenital facial palsy, congenital ptosis with antimongoloid slant, albinotic child with hypochromic iris**



**Figure 3: Fundus picture showing retinitis pigmentosa and pigmentary retinopathy**

## RESULTS

A total of 359 hearing impaired students were examined; males comprised 211/359 (58.8%). Females were 148/359 (41.2%). In this study, 255/359 (71%) had a normal ophthalmologic examination, while 104/359 (29%) had one or more ocular problems. Thus, the prevalence of ophthalmic disorders is 29% in this study. Out of those affected, males were 57/104 (54.8%) and females were 47/104 (45.2%). Refractive errors predominated with the prevalence of 16.99% (61/359). Myopia was found in 49/61 (80.4%) children including myopic astigmatism. Hypermetropia was found in 12/61 (19.6%). With appropriate spectacle correction, 45 had best corrected visual acuity equal to 6/6, 12 had 6/9 and 4 had <6/36 with correction. Pigmentary retinopathy was the most common finding 18/104 (17.3%). Retinitis pigmentosa was diagnosed in 6 (5.76%) children. Heterochromia iridis was present in 8/104 (7.69%) children (Table 1 and Figures 1,3).

Others included conjunctival nevi, microcornea, vernal keratoconjunctivitis (VKC), occlusio pupillae, and optic atrophy. There was a child with right congenital facial

**Table 1: Gender distribution of ocular findings in our study**

Condition	Children (n)	Percentage	Males (n)	Females (n)
Refractive errors	61	58.6	36	25
Pigmentary retinopathy	18	17.3	7	11
Retinitis Pigmentosa	6	5.76	2	4
Heterochromia irides	8	7.69	5	3
Vitamin A deficiency	11	10.57	8	3
DRS+strabismus	3	2.88	3	0
Ptosis	4	3.84	2	2
Hypertelorism	3	2.88	3	0
Nystagmus	3	2.88	2	1
Hordeolum	2	1.92	2	0
Others	12	11.53	6	6

**Table 2: Distribution of ophthalmic manifestations**

Ophthalmic disorder	Number % (n=104)
Preventable	
Vitamin A deficiency (Bitot's spots)	11 (10.57)
Treatable	
Refractive errors	61 (58.6)
Lid problems	7 (6.73)
Strabismus related	3 (2.88)
Unavoidable	
Retinal problems	
Retinitis pigmentosa	6 (5.76)
Pigmentary retinopathy	18 (17.3)
Heterochromia irides	8 (7.69)
Nystagmus	3 (2.88)
Hypertelorism	3 (2.88)
Microcornea	1 (0.96)
Others	10 (9.61)

**Table 3: Comparison of ophthalmic abnormalities with similar studies**

Author	Country	Year	Cases	Ocular problems (%)	Refractive errors (%)
Nicol and House <sup>5</sup>	Australia	1988	78	33	-
Ma <i>et al.</i> <sup>6</sup>	China	1989	279	35.8	17.9
Elango <i>et al.</i> <sup>7</sup>	Malaysia	1994	165	57.6	13.9
Siatkowski <i>et al.</i> <sup>8</sup>	USA	1994	54	61.1	44.4
Guy <i>et al.</i> <sup>9</sup>	UK	2003	122	90.1	31.1
Hanioglu-Kargi <i>et al.</i> <sup>10</sup>	Turkey	2003	104	40.4	29.3
Gogate <i>et al.</i> <sup>3</sup>	India	2008	901	24	18.5
Our study	India	2016	359	29	16.99

palsy with lagophthalmos and another with an artificial eye (Figure 2). Findings do not equal the total number of children as one or more findings are found in a single child. Among the ophthalmic abnormalities, congenital causes are found in 49 children with ptosis and strabismus being the treatable conditions. Acquired causes are found in 75 children with 64 being treatable (refractive errors, hordeolum, and VKC) and 11 being preventable (Vitamin A deficiency). More than 70% of ophthalmic abnormalities are either preventable or treatable in our study (Table 2).

## DISCUSSION

It has been reported that 10% of the Indian children below 14 years of age have some kind of an impairment or physical disability. This mandates a responsible and effective role of the government and its society. It has been estimated that more than half of the total disabilities are preventable by timely intervention at an early stage. An estimated 1-3/1000 children have some degree of sensorineural hearing loss, which occurs as a result of damage to the nerves of the inner ear. Especially early in life, sensorineural hearing loss is associated with delays in language, speech, cognitive, and social development. Given the effects of hearing impairment, children with sensorineural hearing loss are particularly dependent on other means of information acquisition. If these children were to have unrecognized ophthalmologic abnormalities that limited visual acuity, there could be further detrimental effects on development. The results of our study correlate well with other studies as shown in the table. Males comprised 58.8% in our study in comparison to 61.5% in Gogate *et al.* study.<sup>3</sup> The prevalence of ophthalmic disorders was 29% in this study, in comparison to 24% in Gogate *et al.* study.<sup>3</sup> Refractive errors predominated with the prevalence of 16.99%. The prevalence of refractive errors in normal schools is 6.3%.<sup>4</sup> Comparison of ophthalmic abnormalities

in similar studies in hearing impaired children is as shown in Table 3.

Usher's syndrome was seen in 5.76% children in our study in comparison to 4.9% in Guy *et al.* study. Motility disorders were 3.7% in Siatkowski *et al.* study and 1.3% in Gogate *et al.* study in comparison to 2.88% in our study.<sup>3,8</sup>

## CONCLUSION

The prevalence of ophthalmic disorders in hearing impaired schools is more compared to normal schools. Visual impairment in these children can be prevented by regular eye screening by an ophthalmologist and early recognition and treatment of the disorder.

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# Patient-controlled Analgesia with Epidural Bupivacaine-Fentanyl Combination for Labor Analgesia

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## Abstract

**Background:** Pain relief to the parturient in labor is one of the prime responsibilities of the anesthesiologist. Today with the availability of continuous epidural analgesia, we are able to achieve this goal with the patient satisfaction.

**Aim:** To evaluate the efficacy of bupivacaine-fentanyl combination in alleviating labor pain, study its effects on mother and fetus and progress of labor and delivery.

**Materials and Methods:** A total of 100 cases were selected at random and grouped 50 cases and 50 controls each. Satisfactory block was established with continuous epidural analgesia using initial loading dose of 10 ml of 0.25% bupivacaine with 50 µg of fentanyl followed by background infusion of 0.125% bupivacaine with 0.5 µg/ml of fentanyl, 10 ml/h. A patient-controlled analgesia dose of 5 ml with the lockout interval of 15 min was set. The patient's pulse, blood pressure, fetal heart rate, level of sensory analgesia, intensity of motor blockade, and sedation score noted. The nature of uterine contractions, duration of the first, second, and third stage, any complications during labor, nature of delivery, APGAR score were noted in both case and control groups.

**Results:** Labor analgesia was excellent in 70% of the cases and good in 22% of the patients.

**Conclusion:** We conclude that the patient-controlled continuous lumbar epidural analgesia with low dose bupivacaine-fentanyl combination provides effective pain relief during labor.

**Key words:** Bupivacaine, Fentanyl, Labor analgesia, Patient-controlled analgesia pump

## INTRODUCTION

In 1929, Haggard wrote, "The position of woman in any civilization is an index of the advancement of that civilization; the position of woman is gauged best by the care given to her at the birth of her child."<sup>1</sup> The Western civilization made a giant leap on January 19, 1847, when James Young Simpson used diethyl ether to anesthetize a woman with a deformed pelvis. John Snow anesthetized

Queen Victoria for the delivery of Prince Leopold and Princess Beatrice which made labor analgesia popular among layman.<sup>2</sup>

Childbirth is a very painful process. It represents the most common form of acute severe pain in adult life. The severity compared to that of causalgia, cancer pain, and amputation of digits and expressed as the worst pain experienced by the patient.<sup>3</sup> The vast majority of women in labor request pain relief. Failure to provide pain relief results in severe psychological trauma that lasts one's lifetime. It is the prime duty of the caregiver to provide analgesia during labor.<sup>4</sup>

In the first stage of labor, pain is caused by uterine contraction, stretching of lower uterine segment, and dilatation of cervix. Pain impulses are carried through T10

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to L1 fibers. In the second stage, additional pain impulses due to distention of vaginal vault and perineum are carried via pudendal nerve fibers, S2 to S4.<sup>5</sup>

Well-conducted labor analgesia, in addition to relieving pain, provides greater benefit to the mother. Pain will result in maternal hypertension and reduce uterine blood flow. Epidural analgesia blunts the increase in maternal cardiac output, heart rate, and blood pressure that the results with uterine contractions. Epidural analgesia reduces the release of catecholamines due to stress of labor and helps to convert a previously dysfunctional labor to become normal. It eliminates maternal hyperventilation and thereby prevents the leftward shift of fetal oxyhemoglobin dissociation curve.<sup>5</sup>

Lumbar extradural analgesia was described, in 1928, and was popularized by Hingson.<sup>6</sup> Regional analgesia provides pain relief and allows the parturient to remain awake and participate in labor and delivery. Compared to inhalational anesthetics, regional anesthesia is less likely to produce drug-induced depression in the fetus or aspiration pneumonitis in the mother. Continuous infusions of low concentration of local anesthetic into the epidural space provide continuous stable analgesia without fluctuations in pain relief. It allows the mother to be ambulant.<sup>7</sup> The advent of continuous epidural catheters and lipid soluble potent opioids like fentanyl has revolution patient management and labor analgesia in particular. Patient-controlled infusions using patient-controlled analgesia (PCA) pumps offer the patient a better control over pain.

### Aim

To evaluate the efficacy of bupivacaine-fentanyl combination in alleviating labor pain, study its effects on mother and fetus and progress of labor and delivery.

## MATERIALS AND METHODS

The randomized prospective controlled study was done in the Department of Anaesthesiology, Government Rajaji Medical College, Madurai, affiliated to the Tamil Nadu, Dr. M.G.R. Medical University, obtaining approval from the institutional ethical committee. Written informed consent was obtained from the patient and relatives after explaining the procedure. The study involved 100 patients in active labor with singleton pregnancy with vertex presentation at term belonging to American Statistical Association 1 category. The exclusion criterion includes women with cardiac or respiratory diseases, patients who have received systemic opioids in early labor, spinal deformities, bleeding disorders, local sepsis, and high-risk pregnancies. Parturient was selected in random to case and control groups. The control group was not given any analgesia and was well matched with the case group.

Evaluation of medical and obstetric condition of the patient was done. The patient weight and height were recorded. The patient was explained about the procedure, the usage of infusion pump (PCA PUMP), and description of the 10 point visual analog scale (VAS) given. Obstetrician recorded the nature of uterine contraction, cervical dilatation, station of fetal head, and the fetal heart rate. Under all aseptic precautions, epidural was established in L<sub>2-3</sub> or L<sub>3-4</sub> space. A test dose of 3 ml of 1.5% bupivacaine with epinephrine 5 µg/ml was given. Satisfactory block was established with the initial loading dose of 10 ml of 0.25% bupivacaine with 50 µg of fentanyl. The loading dose was further adjusted according to the height of the patient to establish a block of T<sub>10</sub> level.

PCA pump was connected to the epidural catheter. A background infusion of 0.125% bupivacaine with 0.5 µg/ml of fentanyl, 10 ml/h was set. A PCA dose of 5 ml of above preparation with the lockout interval of 15 min was set. In our study, we used the Becton-Dickinson's advanced PCA infuser syringe-based programable infusion system for drug delivery. During the second stage of labor when perineal analgesia is desired, 0.25% bupivacaine 8-10 ml is given in either semi-recumbent or sitting position.

The patient's pulse and fetal heart rate were continuously monitored. Maternal blood pressure was monitored every 5 min using noninvasive blood pressure monitoring device. The level of sensory analgesia and intensity of motor blockade was assessed at half hourly intervals. The frequency of uterine contractions and nature of cervical dilatation and position of head of fetus were monitored. Pain was evaluated using a 10 point VAS with 0-2 (excellent), 3-4 (good), 4-6 (satisfactory), 6-8 (slight), and 8-10 (poor) scoring of quality of pain relief. Sedation was evaluated using modified Ramsay sedation score and motor blockade using Bromage scale.

The following obstetric parameters are noted:

1. Duration and frequency of uterine contractions recorded every 15 min
2. Rate of cervical dilatation and progress of labor
3. Duration of first, second, and third stage of labor
4. Mode of delivery
5. APGAR score.

The patient was monitored for full cervical dilatation. If the second stage is prolonged more than 3 hours in primigravida and 2 hours in multigravida,<sup>8</sup> delivery was assisted with forceps delivery. As the baby is born, APGAR score was noted and neonatal outcome recorded by a pediatrician, duration of the third stage was noted.

In the control group, maternal and fetal parameters are noted. The nature of uterine contractions, duration of

the first, second, and third stage, any complications during labor, nature of delivery, APGAR score were noted in both case and control groups.

## RESULTS

There was no statistical difference between the case and control groups with variables such as age, height, and weight. Of 50 patients in the case group, 35 patients (70%) had excellent pain relief and 11 patients (22%) had good pain relief. Patients with VAS score of more than four were considered to have satisfactory analgesia (8%) (Table 1).

The amount of drug bupivacaine used in primigravida was between 56 mgs and 118.25 mgs with mean of 76.69 mgs, whereas, in multigravida, the range was between 50 mgs and 96.5 mgs with mean of 72 mgs. The amount of fentanyl used in primigravida was between 62.5 µg and 87.5 µg with the average mean of 71 µg, and in multigravida, the range was between 60 µg and 78.75 µg with average mean of 68.6 µg. Labor analgesia was excellent in 70% of the cases and good in 22% of the patients.

The mean rate of cervical dilatation in primigravida (case) group was 2.48 cm, whereas, in primigravida (control) group, it was 1.63 cm. The difference was statistically significant. In the multigravida, case group was 2.96 cm when compared to control group of 2 cm; the difference was statistically significant  $P < 0.05$ .

**Table 1: Quality of pain relief**

VAS	Cases (%)
0-2 excellent	35 (70)
2-4 good	11 (22)
4-6 satisfactory	4 (8)
6-8 slight	-

VAS: Visual analog scale

The duration of the first stage of labor (active phase) in the primigravida (case) group was between 90 min and 315 min with average mean duration of 216 min ( $\pm 49.11$ ). The duration in primigravida (control) group was between 105 min and 640 min with the mean duration of 323 min ( $\pm 180.78$ ). The difference was statistically significant.

In the multigravida (case) group, it was between 90 min and 225 min with the mean duration of 145 min, whereas, in the multigravida (control) group, it was between 75 min and 570 min with the mean duration of 248 min ( $\pm 114.85$ ). The difference was statistically significant. The duration of the first stage of labor (active phase) was shorter in the case group when compared to the control group. The duration of the second stage of labor in both primigravida and multigravida in the case group was prolonged when compared to control group, but the difference was not statistically significant  $P > 0.05$ .

The duration of third stage of labor was similar between the case and control groups in both primigravida and multigravida; and the difference was not statistically significant  $P > 0.05$ .

The total duration of labor in the primigravida (case) group was between 121 min and 420 min with an average mean duration of 273.76 min ( $\pm 55.61$ ), whereas, in the control group, the range was between 127 min and 730 min with the average mean of 368.45 min ( $\pm 24.25$ ). The duration of labor was reduced in the case group, and it was statistically significant. The duration of labor in multigravida (case) group was between 110 min and 317 min with an average mean duration of 182.32 min ( $\pm 36.91$ ). In the control group, it was between 88 min and 656 min with an average mean of 276.45 min ( $\pm 15.44$ ). The duration of labor in the multigravida (case) group was reduced when compared with the control group (Table 2).

**Table 2: Duration of labor**

Stages of labor	Control		Case		P value
	Range	Mean	Range	Mean	
First stage of labor					
Primigravida	105-640	323 $\pm$ 180.78	90-135	145 $\pm$ 38.83	<0.05
Multigravida	75-570	248 $\pm$ 114.85	90-225	248 $\pm$ 114.85	<0.05
Second stage of labor					
Primigravida	20-72	37.85 $\pm$ 20.9	27-90	52.04 $\pm$ 18.84	<0.05
Multigravida	11-70	24.76 $\pm$ 12.8	17-55	32.56 $\pm$ 10.23	<0.05
Third stage of labor					
Primigravida	2-15	6.6 $\pm$ 3.3	4-15	5.72 $\pm$ 2.32	<0.05
Multigravida	2-16	5.7 $\pm$ 3.4	3-7	4.76 $\pm$ 0.83	<0.05
Total duration					
Primigravida	127-730	368.45 $\pm$ 24.25	121-420	273.76 $\pm$ 55.61	<0.05
Multigravida	88-656	279.46 $\pm$ 15.44	110-317	182.31 $\pm$ 6.91	<0.05

About 64% of primigravida (case) group and 80% of primigravida (control) group had normal deliveries. In multigravida, 88% of both case and control groups had normal deliveries. Forceps delivery was conducted for 36% of primigravida (case) group, of which, 20% had outlet forceps and 16% had Lead Maternity Care forceps delivery. In the control group, only 12% of the patients had forceps delivery. In the multigravida group, both the case and control groups had similar forceps delivery of 12%. Lower-segment cesarean section was done in two cases of the primigravida (control) group (Table 3).

Urinary retention was the most common complication occurring during epidural analgesia (60%) followed by nausea and vomiting in 22% of cases. In the control group, 30% of patients had urinary retention and 10% had nausea and vomiting.

## DISCUSSION

Regional blocks for labor and vaginal delivery are the most commonly used technique for pain relief in labor. When administered properly, regional analgesia has no serious maternal or neonatal complications.<sup>2</sup> It does not impede the progress of the first stage of labor.

Continuous infusion of low concentrations of local anesthetic into the epidural space provides continuous, stable anesthetic levels, avoiding fluctuations in pain relief often found with conventional intermittent epidural injections during labor.<sup>7</sup> Because dilute local anesthetic concentrations are used (0.125% bupivacaine), the amount of motor blockade is reduced. Hence, the pelvic muscle tone is maintained and better expulsive forces during the second stage of labor.

During the second stage of labor, 0.25% bupivacaine 8-10 ml was used. This was supported by studies done by Capogna *et al.*,<sup>8</sup> 1998, who noted that increased concentration of local anesthetic is required in second stage of labor. The authors attributed this to compression of pelvic structures by the fetal presenting part resulting in increased frequency of stimulation of A delta fibers.

Porter *et al.*,<sup>9</sup> in 1996, noted that addition of fentanyl to bupivacaine allows the use of reduced concentration of bupivacaine without compromising analgesia and achieving a reduction in motor block. McCoy *et al.*,<sup>10</sup> 1993, concluded that continuous infusions increase dosage without improving pain.

Chumbley *et al.*,<sup>11</sup> in 1999, studied regarding PCA use. They found that patients felt extremely positive about PCA and not worrying about giving oneself too much of a drug.

**Table 3: Mode of delivery**

Mode of delivery	Primigravida		Multigravida	
	Case (%)	Control (%)	Case (%)	Control (%)
Labor natural	64	80	88	88
Outlet forceps	20	8	12	12
LMC forceps	16	4	-	-
LSCS	-	8	-	-

LMC: Lead Maternity Care, LSCS: Lower-segment cesarean section

PCA allows patients to titrate the analgesics to relieve pain, better pain relief, and control over pain. No clear strategy was expressed for pressing or not pressing the PCA button, and the principle of control of pain by the patient was questioned. In our study, patients felt positive about pain relief and PCA.

Russell and Reynolds<sup>12</sup> (1996) have conducted similar study and reported 85% of the patient having good quality analgesia with opioid-bupivacaine combination. In our study, 92% of patients had effective pain relief. Russell and Reynolds found perineal pain in 21% of cases, more so in primigravida. The authors concluded that higher concentrations of 0.25% bupivacaine to relieve perineal pain.

Chestnut and associates<sup>13</sup> have reported that continuous infusion of 0.0625% bupivacaine with 2 µg of fentanyl given to primipara did not prolong but tended to decrease the duration of active phase of first stage of labor.

Fogel<sup>14</sup> (1997) had shown that epidural analgesia does not increase the rate of cesarean delivery.

In our study, the APGAR score in both study and control groups were similar in both primigravida and multigravida. Fernando *et al.*<sup>15</sup> (1997) found that there was no correlation between APGAR score, umbilical blood gases, and umbilical venous concentration of either fentanyl or bupivacaine.

## CONCLUSION

We conclude that patient-controlled continuous lumbar epidural analgesia with low dose bupivacaine-fentanyl combination provides effective pain relief during labor. PCA has added advantage for the patient has control over pain with minimal side effects.<sup>16</sup>

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# Comparison of Chemotherapy Alone with Chemotherapy Plus Rituximab for Treatment of Non-Hodgkins Lymphoma of All Ages and All Histological Subtypes

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## Abstract

**Introduction:** The present day recommendations for treatment of non-Hodgkins lymphoma (NHL) patients is chemotherapy based on cyclophosphamide, doxorubicin, vincristine, and prednisolone with the addition of rituximab for those with cluster designation 20 positive tumors in selected ages and histologic subtypes. Rituximab has shown a favorable effect on the outcome of patients in these subsettings.

**Purpose:** We did a study to analyze the impact of rituximab added to the same chemotherapy on the outcome of NHL patients irrespective of age and histologic subtypes.

**Methods:** The case records of all NHL patients registered in our department from 2008 to 2013 were analyzed. The clinical, histopathological, and treatment details were noted. Comparison was done between patients having received rituximab-based chemotherapy with those who received chemotherapy alone.

**Results:** Of the 94 cases of NHL registered in our department over a 6 year period, 68 patients received chemotherapy in our department with different regimens. 36 patients received monoclonal antibody rituximab added to chemotherapy. The outcome of patients who received rituximab with chemotherapy with respect to complete response, event-free survival (EFS), and overall survival was significantly higher than those who received chemotherapy alone.

**Conclusion:** Addition of rituximab to chemotherapy increases the response rate, prolongs EFS, and overall survival in patients of all ages and histologic subtypes with NHL.

**Key words:** Chemotherapy, Event-free survival, Non-Hodgkins lymphoma, Overall survival, Response rate, Rituximab

## INTRODUCTION

Non-Hodgkins lymphoma (NHL) incidence rates vary over the globe with highest rates in United States, Europe, and Australia, and lowest rates reported from Asia. The cause of most cases of NHL is unknown although several genetic diseases, environmental agents, and infectious agents have

been associated with the development of lymphoma. The present day term NHL can no longer be considered as a single disease or an adequate diagnosis because as per the 2008 World Health Organisation classification of tumors of hematopoietic and lymphoid tissues, 86 distinct entities plus additional variants are included under the lymphoma category,<sup>1</sup> with more than 25 histologic subtypes of B-cell lymphoma having a wide range of biologic and clinical features.<sup>2</sup>

The cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP) regimen is the standard of care for patients with NHL,<sup>3</sup> but it induces complete responses in only 40-50% of patients, with 3-year event-free and overall survival rates of 30% and 35-40%, respectively.<sup>4</sup>

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In many studies,<sup>5</sup> addition of rituximab, a chimeric anti-cluster designation 20 (CD 20) monoclonal antibody to chemotherapy regimen of CHOP in patients with CD 20 positive tumors has significantly increased the rate of complete response, decreased the rates of treatment failure and relapse, and improved event-free and overall survival as compared with standard CHOP alone. However, these results have been seen only in elderly patients with newly diagnosed diffuse large B-cell lymphoma. Similarly also seen,<sup>6</sup> it is an improvement in overall response rates with rituximab added to chemotherapy for patients with low grade (follicular) lymphoma.

In this study, we compared chemotherapy alone with chemotherapy plus rituximab for CD 20 positive NHL patients of all ages and all histologic subtypes with an emphasis on the effect of rituximab on response, event-free survival (EFS), overall survival, and toxicity profile.

## MATERIALS AND METHODS

Case records of all patients with a histopathological diagnosis of NHL registered in our department from 2008 to 2013 (both years included) were taken for the study. Details included registration number, age, sex, residence, clinical presentation, performance status, histopathological subtype, immunohistochemical analysis, type of treatment received, posttreatment outcome, and the last follow-up with special reference to response rates achieved and impact of rituximab on the EFS in these patients. All patients were subjected to a staging workup consisting of contrast-enhanced computerized tomography (CECT) of the neck, chest and abdomen, bone marrow biopsy, laboratory studies to determine renal, hepatic and marrow function, lactate dehydrogenase levels, and hepatitis serology. Cardiac function was evaluated by echocardiography. Only two patients had a positron-emission tomography (PET)-CT done in view of nonavailability of this modality in our state, even though all patients were made aware of the necessity of doing it. In 23 patients, disease was upstaged by CECT from clinical Stage I to Stage III and in two patients by PET-CT from Stage I to Stage III. Out of a total of 94 patients registered, only 68 patients were treated in our department plus 1 patient who had stage Is disease and was put on follow-up alone (total of 69 patients). Among those not treated, 15 patients absconded after registration only, 3 pediatric patients with Burkitt's lymphoma were referred to medical oncologist at the Sher-i-Kashmir Institute of Medical Sciences, and 7 patients had already received chemotherapy and/or radiotherapy at other centers before getting registered with us and all these absconded without receiving any treatment in our department.

## Treatment

For these 68 patients, chemotherapy in different schedules was administered. The regimens included CHOP in 32 patients, rituximab, CHOP in 35 patients, and rituximab, high-dose systemic methotrexate, CHOP in 1 patient with testicular lymphoma. Patients treated with CHOP received the combination of 750 mg of cyclophosphamide/m<sup>2</sup> of body-surface area on day 1; 50 mg of doxorubicin/m<sup>2</sup> on day 1; 1.4 mg of vincristine/m<sup>2</sup>, up to a maximal dose of 2 mg, on day 1; 16 mg of dexamethasone each on day 1 and day 2 (the equivalent of 100 mg of prednisone daily); 40 mg of prednisone m<sup>2</sup>/day from day 3 to day 5. Patients treated with CHOP plus rituximab also received rituximab, at a dose of 375 mg/m<sup>2</sup>, in two divided doses on day 1 and day 2 for all patients for first two cycles and for first four cycles for elderly and those with bulky disease. One patient received 3 g of methotrexate given intravenously over 6 h with leucovorin rescue. All the regimens were given for a total of 6 cycles at 3 weekly intervals. Although all eligible patients were offered rituximab, only 36 patients agreed and received it in combination with different chemotherapy regimes, whereas 32 patients received chemotherapy without rituximab.

Radiotherapy was used where ever it was indicated. Based on whether they received rituximab or not, they were grouped into two groups. Group I included those who did not receive rituximab with chemotherapy (nonrituximab group), and Group II included those who received rituximab with chemotherapy (rituximab group) (Table 1). Response to treatment and adverse events tumor responses were assessed after six cycles of chemotherapy as complete response, unconfirmed complete response, partial response, stable disease, or progressive disease according to the International Workshop criteria.<sup>7</sup> Complete response was defined as the disappearance of all lesions observed at diagnosis and the absence of new lesions. An unconfirmed complete response was defined as a complete response with the persistence of some radiologic abnormalities, which had to have regressed in size by at least 75%. Partial response was defined as the regression of all measurable lesions by more than 50% and the absence of new lesions. Stable disease was defined as a regression of any measurable lesion by 50% or less but without growth of existing lesions or the appearance of new lesions. Progressive disease was

**Table 1: Distribution of patients according to treatment received**

Total number of patients receiving treatment	Group I (nonrituximab group)	Group II (rituximab group)
68	32	36

defined as the appearance of a new lesion, any growth of the initial lesion by more than 25%, or growth of any measurable lesion that had regressed during treatment by more than 50% from its smallest dimensions.

All adverse events reported by the patient were collected from the case reports. An adverse event was defined as any adverse change from the patient's base-line condition, whether related to treatment or not. Each event was graded according to the National Cancer Institute Common Toxicity Criteria grading system.<sup>8</sup> Only Grade 3 and 4 events plus Grade 2 infections were recorded in detail, whereas Grade 1 and 2 adverse events were disregarded.

### Statistical Analysis

Data were analyzed using SPSS version 20.0. Categorical variables were summarized as percentages. 95% confidence intervals were reported. Event-free and overall survival was assessed using Kaplan–Meier analysis. Mean survival time along with its 95% confidence interval was reported. The difference in survival times of CHOP versus Rituximab plus CHOP were analyzed by the log-rank test. Two-tailed *P*-values were reported, and a *P* < 0.05 was considered statistically significant.

## RESULTS

The baseline characteristics of the patients in the two groups were compared (Table 2). There was no significant difference between the two groups in any clinical or pathological characteristic. The age distributions of the two groups showed that the majority of patients in both groups were <60 years and gender wise; the two groups were nearly equally matched.

The presence of B symptoms was noted in around 40% and 34% of patients of Groups I and II, respectively. Except one patient, whose histopathology was T-cell type, all others were B-cell lymphomas. Among the B-cell lymphomas, the majority of patients had diffuse large B-cell lymphoma followed by follicular type. All the patients were staged as per Ann Arbor staging system, and international prognostic index score was used for prognostication of patients in the two groups.

We followed the patients in the two groups regularly noting the time duration, for which they were event free after completing treatment. We observed that among patients of Group I, out of a total of 32 patients, 21 patients (66%) are disease free, alive, and on follow-up, whereas, in Group II, out of a total of 36 patients, 29 patients (81%) are disease free, alive, and on follow-up till cutoff date (December 2013). During this time, 11 events (relapse, death, and

progression) were observed in Group I and 7 in Group II (34% and 19% of patients, respectively) (Table 3).

Event-free survival was slightly longer for patients of Group II than for Group I though the value did not have statistical significance (*P* = 0.295) (Table 4 and Figure 1). The difference in EFS between the treatment groups was attributable to the higher number of patients (nearly double) in Group I having disease relapse. There was benefit of rituximab, for all patients irrespective of bulk of disease, presence of B symptoms and age (data not shown).

In Group I, complete response was achieved in 53%, partial response in 9%, and stable disease in 3% of patients as compared with Group II where the complete response was achieved in 61%, partial response in 13%, and stable disease in 5%. Disease progression during treatment was reported in 1 patient each in Group I and II (Table 5). The rate of objective response was 62.5% and 75% in

**Table 2: Characteristics of patients in the two groups**

Characteristic	Group I (n=32) (%)	Group II (n=36) (%)
Age (years)		
≤60	22 (68)	23 (64)
61-70	06 (18)	09 (25)
>70	04 (12)	04 (11)
Gender		
Male	20 (62)	23 (64)
Female	12 (38)	13 (36)
B symptoms <sup>‡</sup>	14 (44)	12 (33)
Histopathology		
Diffuse large cell	25 (78)	29 (80)
Follicular	06 (19)	07 (19)
NK T-cell	01 (3)	0 (0)
Stage		
1	5 (15)	04 (11)
2	6 (19)	06 (17)
3	14 (44)	15 (42)
4	07 (22)	11 (30)
International prognostic index score		
Low (0-1)	09 (28)	07 (19)
Low intermediate (2)	14 (44)	13 (36)
High intermediate (3)	05 (16)	10 (28)
High (4-5)	04 (12)	06 (17)

<sup>‡</sup>B symptoms were defined as weight loss, fever, and night sweats. NK: Natural killer

**Table 3: Status of patients in both groups at the end of study**

Event	Group I (n=32)	Group II (n=36)
Alive and disease free <sup>‡</sup>	21 (66)	29 (81)
Relapse <sup>‡</sup>	06 (19)	03 (8)
Death <sup>‡</sup>	04 (12)	03 (8)
Progression <sup>‡</sup>	01 (3)	01 (3)

<sup>‡</sup>Figures in parentheses are % age

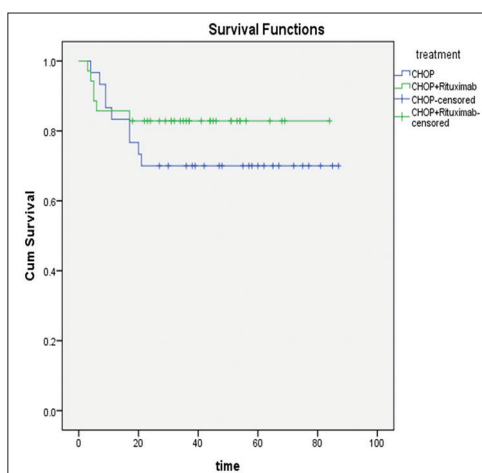
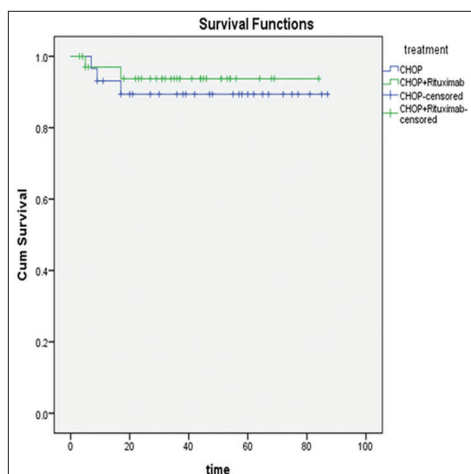
**Table 4: Mean event-free survival time in the treatment groups**

Treatment	Mean	Standard error	95% confidence interval		P (Log-rank test)
			Lower bound	Upper bound	
CHOP	64.733	6.236	52.510	76.957	0.295
CHOP+rituximab	70.743	4.938	61.065	80.420	
Overall	69.268	4.031	61.368	77.167	

**Table 5: Response to treatment in the two groups**

Response	Group I (n=32)	Group II (n=36)
Complete response	17	22
Partial response	03	05
Stable disease	01	02
Progressive disease	01	01
Rate of objective response <sup>a</sup>	62.5% (45–79)	75% (60–89)
		P=0.2665

<sup>a</sup>Figures in parenthesis indicate 95% CI for rate of objective response. 95% CI for difference between rate of objective response among the two groups=9.19–33.09

**Figure 1: Event-free survival among 68 patients assigned to chemotherapy or chemotherapy plus rituximab****Figure 2: Overall survival among 68 patients assigned to chemotherapy alone or with rituximab**

Group I and in Group II, respectively, with a  $P = 0.2665$ . Survival was longer for patients of Group II than for those

of Group I although it was not statistically significant ( $P = 0.599$ ) (Figure 2).

### Adverse Effects

Table 6 presents all reported adverse events in each group. The Grades 3 and 4 adverse events were consistent with the expected toxic effects of CHOP chemotherapy and occurred with similar frequency in both groups. The occurrence of infusion-related events such as respiratory symptoms, chills, fever, and hypotension has been known with rituximab administration,<sup>9-11</sup> but we did not see such reactions because we divided the dose of rituximab over 2 days for first two cycles for all patients and for first four cycles in elderly patients and those with bulky disease. In addition, the infusion of rituximab was given slowly to all patients. The median fall of the neutrophil count after each cycle of chemotherapy was similar in both groups. The percentages of patients who required treatment with granulocyte colony-stimulating factor increased to a similar degree in each treatment group.

All adverse events reported by the patient or observed by the investigator were recorded. An adverse event was defined as any adverse change from the patient's base-line condition, whether it was considered related to treatment or not. Each event was graded according to the National Cancer Institute Common Toxicity Criteria grading system; higher numbers denote more severe toxicity.

### DISCUSSION

In this study, we analyzed the data of NHL patients treated in our department with emphasis on the efficacy and safety of rituximab in combination with CHOP chemotherapy in patients of all ages and all histological subtypes. We found higher response rates, improved EFS, and overall survival (though not statistically significant) among patients treated with the combination of rituximab and chemotherapy irrespective of age and histologic subtype. The longer EFS in Group II was due to a lower rate of disease relapse among patients who had a complete response. Treatment with chemotherapy plus rituximab was well tolerated, and the incidence of severe or serious adverse events was no different from that in the chemotherapy alone group. The most common infusion-related effects

**Table 6: Adverse events observed in patients treated with CHOP plus rituximab or CHOP alone**

Neutropenia
Fever
Infection
Mucositis
Liver toxicity
Cardiac toxicity
Neurologic toxicity
Renal toxicity
Lung toxicity
Nausea or vomiting
Alopecia

CHOP: Cyclophosphamide, doxorubicin, vincristine, and prednisone

seen almost universally were not experienced by our patients as we divided the dose of rituximab over 2 days for all patients for first two cycles and first four cycles for elderly and those with bulky disease. Furthermore, we gave the glucocorticoid component of CHOP regimen by intravenous route on first 2 days to act as a premedication for decreasing the chances and severity of infusion-related reactions. CHOP chemotherapy is considered a standard and less toxic regimen against which other regimens are to be compared. Hence, it is considered a first-line treatment for NHL patients and the outcome in this study with CHOP alone was the same as in other trials. Hence, the improved results in the group receiving CHOP with rituximab were actually attributable to the effects of rituximab.

## CONCLUSION

In conclusion, the addition of rituximab to CHOP chemotherapy given for six cycles to newly diagnosed NHL patients of all ages and all histologic subtypes increases the rate of complete response, improves event-free, and overall survival as compared with standard CHOP alone. This improvement in outcome was achieved without any significant increase in clinical toxic effects probably due to modifications in the administration schedule of rituximab. Even though our results did not show a significant change statistically, but we believe that incorporating a greater number of patients and doing this study in a multicenter setting may achieve statistically significant and practice-changing results.

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# Prevalence of Dengue Fever in Kanyakumari District: A Cross-sectional Study

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## Abstract

**Introduction:** The global prevalence of dengue has grown dramatically in recent decades. Therefore, a study regarding the prevalence of dengue fever in Kanyakumari district will provide the necessary data to tackle the disease and prevent future outbreaks.

**Aim:** To determine the prevalence of dengue fever in Kanyakumari District, southern coastal district of Tamil Nadu during the period from June to July 2013 and early detection of secondary dengue cases.

**Methods:** A cross-sectional study was conducted in Nagercoil in patients with fever suspicious of dengue referred from various hospitals in Kanyakumari district during June and July 2013. Patients with fever and other associated symptoms such as headache, joint pains, purpuric rashes, and reduction in platelet count were noted. 3 ml of blood is collected aseptically by venipuncture. The serum is subjected to serological tests for dengue immunoglobulin M enzyme-linked immunosorbent assay (ELISA) and immunoglobulin G ELISA (PanBio diagnostics).

**Results:** Among 226 cases suspected for dengue fever, 140 (62%) were positive for dengue and 86 (38%) were negative. Out of 140 positive cases, 61 were primary dengue and 79 cases were secondary dengue. Among the age group, positivity was significantly high (46%) in 0-10 years age group. By clinical evaluation, 35% cases had hemorrhagic manifestations including petechiae, gum bleeding, and epistaxis.

**Conclusion:** The present study has shown the prevalence of dengue fever in Kanyakumari District, southern coastal district of Tamil Nadu. The study has also showed the early diagnosis of secondary dengue to reduce morbidity and mortality.

**Key words:** Dengue, Immunoglobulin G and immunoglobulin M enzyme-linked immunosorbent assay, Kanyakumari, Secondary dengue

## INTRODUCTION

Dengue virus is a mosquito-borne *Flavivirus* and the most prevalent arbovirus in tropical and subtropical regions of the world.<sup>1</sup> Dengue virus is a positive-stranded encapsulated RNA virus. There are four distinct serotypes: Serotypes 1-4. Infection induces a lifelong protective immunity to the homologous serotype but confers only partial and transient protection against subsequent infections by the other three serotypes. Instead, it has generally been accepted that

secondary infection or infection with secondary or multiple infections with various dengue virus serotypes is a major risk factor for dengue hemorrhagic fever-dengue shock syndrome (DHF-DSS) due to antibody-dependent enhancement.<sup>2-4</sup> Dengue is an endemic viral disease affecting predominantly in urban and semi-urban areas. The global prevalence of dengue has grown dramatically in recent decades. The disease is now endemic in more than 100 countries in Africa, America, the eastern Mediterranean, Southeast Asia, and the Western Pacific, threatening more than 2.5 billion people.<sup>5</sup> The World Health Organization estimates that there may be 50 million to 100 million cases of dengue virus infections worldwide every year, which result in 250,000-500,000 cases of DHF and 24,000 deaths each year.<sup>6,7</sup> Dengue virus causes a broad spectrum of illnesses, ranging from inapparent infection, flu-like mild undifferentiated fever, and classical DF to the more severe form, DHF-DSS, from which rates of morbidity and mortality are high.<sup>5,7-9</sup> Dengue virus serotype analysis is

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important in epidemiological and pathological studies. Among the available methods, virus isolation followed by type-specific monoclonal antibody immunofluorescence staining, the neutralization test, and reverse transcription-polymerase chain reaction are widely used by many laboratories studying dengue virus.<sup>7,10</sup> Two patterns of serological response can be observed in patients with dengue virus infection: Primary and secondary antibody responses depending on the immunological status of the infected individuals. A primary antibody response is seen in individuals who are not immune to *Flaviviruses*. A secondary antibody response is seen in individuals who have had a previous *Flavivirus* infection. For acute- and convalescent-phase sera, serological detection of antibodies based on capture immunoglobulin M (IgM) and immunoglobulin G (IgG) enzyme-linked immunosorbent assay (ELISA) has become the new standard for the detection and differentiation of primary and secondary dengue virus infections.<sup>7,11,12</sup> The management of dengue virus infection is essentially supportive and symptomatic. No specific treatment is available. However, there are Indian studies which have contributed in terms of better management of DHF/DSS. A rapid response to platelet and fresh frozen plasma transfusion is reported in a study.<sup>13</sup>

Dengue is one of the major public health problems which can be controlled with active participation of the community. Need is to organize health education programs about dengue disease to increase community knowledge and sensitize the community to participate in integrated vector control programs.<sup>14,15</sup> As attempts to eradicate *Aedes aegypti*, the most efficient mosquito vector of dengue virus, are not successful in countries where dengue is endemic, the control of dengue will be possible only after an efficient vaccine has been developed. At present, no dengue vaccine has been licensed. The development of an efficient dengue vaccine is difficult because the vaccine must be tetravalent so that it includes all four serotypes. The global prevalence of dengue has grown dramatically in recent decades. Therefore, a study regarding the prevalence of dengue fever in Kanyakumari district will provide the necessary data to tackle the disease and prevent future outbreaks.

### Aim

To determine the prevalence of dengue fever in Kanyakumari, southern coastal district of Tamil Nadu, during the period June and July 2013 and early detection of secondary dengue cases.

## MATERIALS AND METHODS

A cross-sectional study was conducted in Nagercoil in patients with fever suspicious of dengue referred from various hospitals in Kanyakumari district during June and July 2013. Patients with fever and other associated symptoms such as headache, joint pains, purpuric rashes,

and reduction in platelet count were noted. 3 ml of blood is collected aseptically by venipuncture. The serum is subjected to serological tests for dengue IgM ELISA and IgG ELISA (PanBio diagnostics).

## RESULTS

Among 226 cases suspected for dengue fever, 140 (62%) were positive for dengue and 86 (38%) were negative. Among the cases tested for dengue by IgM and IgG Capture ELISA, 61 (44%) positive for IgM antibodies only, 18 (12%) were positive for only IgG antibodies and 61 (44%) were positive for both IgM and IgG antibodies. (Table 2). Of 140 positive cases, 61 were primary dengue and 79 cases were secondary dengue. Among the age group, positivity was significantly high (46%) in 0-10 years age group (Table 3). By clinical evaluation, 35% cases had hemorrhagic manifestations including petechiae, gum bleeding, and epistaxis (Figure 1).

## DISCUSSION

As our study was conducted during an outbreak in Kanyakumari district during monsoon period, an unusually high prevalence is seen indicating about 62% positivity. According to Gupta *et al.*, of 1820 serum samples received from suspected cases in all 3 years, 811 (44.56%) were confirmed as dengue infection serologically. There was an increase in the number of samples received in the postmonsoon period (September to November) with a peak in the 2<sup>nd</sup> and 3<sup>rd</sup> week of October.<sup>16</sup>

**Table 1: Sex distribution of clinical cases**

Dengue	Total	Male	Female
Number of patients tested	226	120	106
Number of positive cases	140	70	70

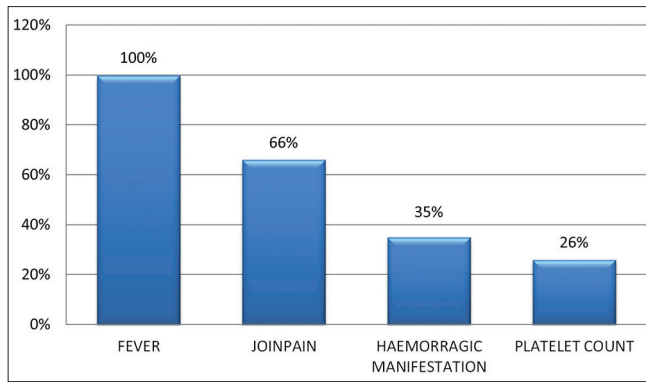
**Table 2: Dengue positive cases**

Test	Dengue positive		
	IgM (%)	IgG (%)	IgM+IgG (%)
Total	61 (44)	18 (12)	61 (44)

**Table 3: Age group of dengue cases**

Age group	IgM ELISA positive	IgG ELISA positive	IgM and IgG ELISA positive	Total
0-10	36	7	22	65
11-20	4	2	9	15
21-30	6	1	9	16
31-40	4	1	6	11
41-50	4	4	3	11
Above 50	7	3	12	22
Total	61	18	61	140

IgM: Immunoglobulin M, IgG: Immunoglobulin G, ELISA: Enzyme-linked immunosorbent assay



**Figure 1: Signs and symptoms observed in dengue cases**

According to the WHO publication 1997, secondary dengue infection was characterized by high IgG which may be accompanied by elevated IgM levels, and the cases with only IgM positive were considered as primary dengue.<sup>17</sup> Of 140 positive cases, 61 were primary dengue and 79 cases were secondary dengue in our study.

Serological studies, for primary infection, the dominant immunoglobulin isotype is IgM, IgM may appear during febrile phase (50% of cases), the other half, it appears within 2-3 days of defervescence. Once detectable, IgM levels rise quickly and appear to peak about 2 weeks after the onset of symptoms, and then, they decline to undetectable level over 2-3 months. IgG appears shortly afterward with very low level. The physiological definition of a primary infection is, therefore, characterized by a high molar fraction of IgM and low molar fraction of IgG. Secondary dengue infections are characterized by a rapid increase in IgG antibodies, IgM appears in the most instances, the level is dramatically lower.<sup>18</sup>

In our study, positivity was significantly high (46%) in 0-10 years age group. However, in the study by Gupta *et al.* among the confirmed dengue cases, maximum cases were seen in the age group 21-30 years.<sup>16</sup>

In a study by Ali *et al.*, overall male population was mostly infected as compared to females and people in the age group between 15 and 45 was the highest infected group.<sup>17</sup> In our study, among the positive patients, male and female have equal distribution. By clinical evaluation, among the 140 positive cases, 66% patients had joint pain, 35% cases had hemorrhagic manifestations including petechiae, gum bleeding, and epistaxis, and 26% patients had thrombocytopenia in our study.

## CONCLUSION

The present study has shown the prevalence of dengue fever in Kanyakumari District, southern coastal district of Tamil Nadu. The study has also shown the early diagnosis of secondary dengue to reduce morbidity and mortality because patients with secondary infection are more likely to have severe forms of dengue such as DHF-DSS.

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# Comparison of Percutaneous Endoscopic Gastrostomy with Nasogastric Tube Feeding in Patients Suffering from Obstructing Esophageal and Upper Aero-Digestive Malignancies - A Retrospective Analysis

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## Abstract

**Background:** A number of conditions compromise the passage of food along the digestive tract. A nasogastric tube (NGT) feeding is a classic, time-proven technique to provide nutritional support, although its prolonged use can lead to complications. Another method, percutaneous endoscopic gastrostomy (PEG) involves a feeding tube inserted directly into the stomach through the abdomen and is particularly useful when enteral nutrition is needed for a length of time.

**Materials and Methods:** Prospective observational study in which patients with obstructing growth of esophagus and oropharyngeal malignancies with dysphagia and poor oral food intake, who were selected for further treatment under curative or palliative intent with chemo-irradiation were included in the study. Patients who underwent PEG tube insertion as feeding procedure before the onset of treatment were compared with patients who had NGT as the feeding procedure.

**Results:** A total of 26 patients with PEG insertion were compared with control group of 28 patients with NTG tube feeding during the treatment. All patients in the PEG group completed chemo irradiation for 5 or 6 weeks depending on the intent to treat. In the NGT group, 5 patients interrupted treatment due to inadequate hydration and nutrition as a result diminishing performance status and required multiple readmissions during the course of treatment. In PEG group, minor complications, such as small leak and minor, wound infection occurred in 7/26 patients which subsided with treatment. No major side effects like pneumonitis or perforation occurred in this group. One patient had slipped of PEG tube due to the extension of growth into the body of stomach. In NGT group, kinking of NGT occurred in 5/26 patients and so had to be reinserted.

**Conclusion:** The studies showed a higher probability of treatment failure with an NGT. The number of deaths was no different with the two methods, nor was the overall occurrence of adverse events. Patients with PEGs may have a better quality of life.

**Key words:** Nasogastric tube, Obstructing esophageal and upper aero-digestive malignancies, Percutaneous endoscopic gastrostomy

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## INTRODUCTION

A number of conditions compromise the passage of food along the digestive tract. A nasogastric tube (NGT) feeding is a classic, time-proven technique to provide nutritional support, although its prolonged use can lead to complications such as lesions to the nasal wing,

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chronic sinusitis, gastroesophageal reflux, and aspiration pneumonia. Another method, percutaneous endoscopic gastrostomy (PEG) involves a feeding tube inserted directly into the stomach through the abdomen and is particularly useful when enteral nutrition (EN) is needed for a length of time.<sup>1,2</sup>

Conditions associated with swallowing disorders include stroke, neurological diseases, dementia, cancers of the head and neck, amyotrophic lateral sclerosis, physical obstruction, and dysphagia from stroke. The patients with swallowing disturbances can develop low nutritional status, which affects their recovery from illness.

The patients unable to maintain an adequate oral intake have greater rates of weight loss, hospitalization, and forced treatment breaks.<sup>3</sup> Loss of >10% body weight has also been associated with decreased quality of life (QOL).<sup>3,4</sup> Some 40-57% of head and neck cancer patients may be malnourished at presentation,<sup>5</sup> with figures increasing to 88% during the treatment.<sup>6</sup> Causes are multifactorial, with contributions from patient, treatment and tumor factors. EN, delivered via NG or PEG tube, may enable select patients to maintain their weight and minimize toxicity.

### Aim

To evaluate the effectiveness and safety of PEG compared with NGT for patients who were suffering from obstructing growth of the esophagus and upper aero-digestive tract, in terms of nutritional outcomes, complications, patient satisfaction, and cost.

## MATERIALS AND METHODS

Prospective observational study was conducted in the Department of Medical Gastroenterology, Thoothukudi Medical College Hospital. The study was conducted over a period of 3-year from June 2013 to May 2016. The patients with obstructing growth of esophagus and oropharyngeal malignancies with dysphagia and poor oral food intake who were selected for further treatment under curative or palliative intent with chemo irradiation were included in the study. The patients had PEG insertion done as feeding procedure before definitive treatment by chemo irradiation. These patients were compared with a similar control group of patients who were given only NGT feeding as the feeding procedure due to various reasons. All these patients underwent radiotherapy for 5-6 weeks depending on the intent to treat - palliative or curative along with chemotherapy regimens. All patients who were candidates for surgical treatment and who had severe trismus due to primary in retromolar trigone were excluded from the study.

A total of 26 patients underwent PEG insertion in the Department of Medical Gastroenterology, Thoothukudi Government Medical College after 2013 for obstructing malignancies of upper aero-digestive tract.

They were compared with an age-matched control group of 28 patients who were managed only with NGT feeding during the treatment.

## RESULTS

All the study patients were in the age group between 40 and 80, 19 males and 7 females in the PEG group, and 20 males and 6 females in the NGT group. In PEG group, there were 4 oropharyngeal malignancies, 3 postcricoid malignancies, 1 in upper third esophagus, 7 in middle third esophagus, and 11 in lower third esophagus OG junction growth. In NGT group, there were 7 oropharyngeal malignancies, 3 postcricoid malignancies, 7 in middle third esophagus, 9 lower third esophagus. In PEG group, 24 were squamous cell carcinoma. 2 patients had adenocarcinoma involving the lower third esophagus and OG junction who were inoperable and were on palliative chemotherapy. In NGT group, all 26 were squamous cell carcinoma. All patients in the PEG group completed chemo irradiation for 5 or 6 weeks depending on the intent to treat. In the NGT group, 5 patients interrupted treatment due to inadequate hydration and nutrition and as a result diminishing performance status. In the remaining 21 patients, 8 had removed the NGT during the 2<sup>nd</sup> or 3<sup>rd</sup> week of radiation treatment. In 5 of them, NGT was reinserted for nutrition. The remaining 3 had improvement in dysphagia and so they continued radiation therapy (RT) with the adequate oral intake. Only 13 patients kept the NGT *in situ* at the end of 5 weeks of treatment.

Follow-up: PEG group: 4 patients were lost to follow-up, 14 patients expired after completion of treatment after surviving for varying intervals from 2 months to 1 year, 3 patients expired within 3 months. 19 patients survived for more than 3 months after treatment and 8 patients were alive after 1 year. In NGT group, 6 patients were lost to follow-up, 17 patients expired after completion of treatment after surviving for varying intervals from 2-month to 2-year. 19 patients survived for more than 3 months after treatment and 4 patients were alive after 1 year.

Nutrition and performance status: PEG group: Weight loss was seen only in 3 patients. They had the WHO progression-free survival (PFS) of III or IV. All the remaining 23 patients gained a weight of 1-2.5 kg during treatment and maintained the WHO PFS of II. In NGT

Group, weight loss was seen in 5 patients. They had WHO PFS of III or IV. The remaining 21 patients gained a weight of 0.5-1 kg during the treatment and maintained a WHO PFS of II or III.

The patients with PEG did not have any intermittent hospitalization during and immediately after completion of treatment for nutritional supplementations. All patients in the NGT group had to be admitted for 2-3 times during treatment for reinsertion of NGT and for nutritional supplementation.

Long-term follow-up: PEG tube removal was done in 6 patients who had complete clinical response. In 5 of the 8 patients, who survival was more than 1 year, post-RT stricture was seen and so PEG tube removal was not attempted. NGT: 50% patients removed the NGT either during or toward the end of treatment as the dysphagia improved. Only 5 patients completed the treatment with NGT *in situ* and for whom it was removed after completion of treatment.

Adverse events: PEG: Minor complications such as small leak and minor wound infection occurred in 7/26 patients which subsided with treatment. No major side effects like pneumonitis or perforation occurred in this group. One patient had slipped of PEG tube due to the extension of growth into the body of stomach. NGT: Kinking of NGT occurred in 5/26 patients and so had to be reinserted.

The cost of a PEG tube was 10 times that of an NGT.

## DISCUSSION

A number of conditions compromise the passage of food along the digestive tract. NGT feeding is a classic, time-proven technique to provide nutritional support, although its prolonged use can lead to complications such as lesions to the nasal wing, chronic sinusitis, gastroesophageal reflux, and aspiration pneumonia. Another method, PEG involves a feeding tube inserted directly into the stomach through the abdomen and is particularly useful when EN is needed for a length of time.<sup>1,2</sup>

The patients unable to maintain adequate oral intake have greater rates of weight loss, hospitalization, and forced treatment breaks.<sup>3</sup> Loss of >10% body weight has also been associated with decreased QOL.<sup>5-7</sup> Some 40-57% of obstructing malignancies of esophagus and upper aero-digestive tract patients may be malnourished at presentation,<sup>7</sup> with figures increasing to 88% during treatment.<sup>8</sup> Causes are multifactorial, with contributions

from patient, treatment and tumor factors. EN delivered via NGT or PEG tube, may enable select patients to maintain their weight and minimize toxicity.

Our study showed a higher probability of treatment failure with a nasogastric tube, which is consistent with other reported studies. The number of deaths was no different with the two methods; nor was the overall occurrence of complications. However, the QOL and the WHO PS were better in the PEG group compared to the NGT group. The high cost of PEG and requirements for endoscopy limits the use of PEG as it requires a specialized team for insertion. Possible limitations of this review include the small number of participants.

## CONCLUSION

In the patients with obstructing esophageal and upper aero-digestive tract growths, PEG was associated with a lower probability of intervention failure and interruption of nutrition, while NGT has lower rates or morbidity, suggesting the endoscopic procedure may be more effective and safe compared with NGT. There is no significant difference in mortality rates between comparison groups, or in adverse events, including pneumonia related to aspiration. QOL and performance status during treatment were better with PEG tube than NGT, which is very important for the continuation of treatment in these malignancies. In a country like India, most of the patients with esophageal malignancies present with Grade II or III dysphagia with significant weight loss, and so PEG will be a better modality of nutrition in these patients. Future studies should include details of participant demographics including underlying disease, age and gender, and the gastrostomy technique.

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# Postprandial Hypertriglyceridemia as an Independent Risk Factor for Ischemic Heart Disease

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## Abstract

**Introduction:** Atherosclerosis is the leading cause of death and disability in the developed world. Despite our familiarity with this disease, some of its fundamental characteristics remain poorly, recognized, and understood.

**Aim:** To study the relation between risk factors for atherosclerosis using fasting and postprandial triglyceride (TG) levels in patients of unstable angina.

**Materials and Methods:** Observational prospective study on unstable angina patients not on treatment was assessed on serum cholesterol, serum TG, high-density lipoprotein (HDL), low-density lipoprotein (LDL), very LDL, postprandial 2 h glucose, 4 h blood samples for TGs levels.

**Results:** Postprandial hypertriglyceridemia was found in 64%, 52% had high body mass index, 7.3% patients had high waist-hip ratio, and 64% patients had diabetes mellitus.

**Conclusion:** Increased TG level is a risk factor for cardiovascular disease independent of HDL cholesterol level.

**Key words:** IHD, Hypertriglyceridemia, risk factors

## INTRODUCTION

Atherosclerosis is the leading cause of death and disability in the developed world.<sup>1</sup> Despite our familiarity with this disease, some of its fundamental characteristics remain poorly, recognized, and understood.<sup>2</sup> Although many generalized or systemic risk factors predispose to its developments, atherosclerosis affects various regions of the circulation preferentially and yields distinct clinical manifestations depending on the particular circulatory bed affected. The association between atherosclerotic diseases and elevated fasting plasma low-density lipoprotein (LDL)-cholesterol and reduced fasting

plasma high-density lipoprotein (HDL)-cholesterol is well established.<sup>3-6</sup> However, many individuals without fasting lipid abnormalities develop atherosclerotic diseases and several lines of evidence suggest that non-fasting lipid measurements may be more relevant to atherogenesis.<sup>7,8</sup>

## Aim

To study the relation between risk factors for atherosclerosis using fasting and postprandial TG levels in patients of unstable angina.

## MATERIALS AND METHODS

The observational prospective study was conducted in Department of Medicine, Government Mohan Kumaramangalam Medical College Hospital. Approval from Institutional Ethics committee and informed consent from patients were obtained. Patients with unstable angina diagnosed on classical anginal chest pain or anginal chest pain equivalent with electrocardiogram showing ST-

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segment depression in two consecutive chest leads or limb leads and normal serum creatine phosphokinase-MB levels, fasting serum triglycerides (TGs) <150 mg%, fasting serum cholesterol <180 mg% were included in the study. Patients already on treatment for lipid lowering agents, suspected case of Prinzmetal's angina, Rheumatic heart disease, oral contraceptive pills, or other hormone therapy were excluded from the study. Selected patients completed history was taken complete physical and cardiovascular system examination was performed. Laboratory tests serum cholesterol, serum TG, HDL, LDL, very LDL, postprandial 2 h glucose, 4 h blood samples for TGs levels were done.

## RESULTS

A total of 100 patients were included in this study, out of 56 were male and 44 were female. Only 17 female patients are aged <46 years. There were 46 patients in age group 46-55, out of which 27 were male and 19 were female. 32 male and 25 female patients were hypertensive and 34 male and 30 female were diabetes (Table 1).

In our study, 40 patients were overweight, 52 were obese, and only 8 patients had normal weight. 25 male (62.5%) were overweight, 26 male (50%) were obese, 5 male (62.5%) had normal weight. In 44 females, 15 females (37.5%) were overweight, 26 females (50%) were obese, 3 females (37.5%) had normal weight.

About 71% of male and 75% of female patients had high waist-hip ratio (WHR). Out of 100 patients, 64 patients showed serum TG levels >160 mg% after 4 h of meal. 34 out of 56 male patients (60.7%) and 30 out of 44 female (68.18%) showed postprandial hypertriglyceridemia. In this study, 58 patients had low fasting HDL level (<40 mg% in male <50 mg% in female), 36 out of 56 male (64.28%) and 22 out of 44 female (50%) had low fasting HDL level.

In this study, out of 100 patients 64 had postprandial hypertriglyceridemia. Out of 64, 44 had low fasting serum HDL and 20 had normal fasting serum HDL. While 36 patients had normal postprandial serum TG level, out of 36, 14 had low fasting serum HDL and 22 had normal fasting serum HDL. There is no relation found between HDL level and high PP4TG levels ( $P = 0.341$ ) (Table 2).

In this study, out of 76 patients having high WHR; 62 (81.5%) had high PP4TG, while 14 had normal PP4TG. Out of 24 normal WHR patients, 2 had high PP4TG (Table 3).

In this study, out of 32 patients having a high body mass index (BMI), 38 patients (73.07%) had high postprandial TG levels. While out of 40 patients had (60%) high postprandial

TG levels. Moreover, 2 patients out of 8 patients (25%) having normal BMI had high PP4TG levels (Table 4).

In this study, 64 patients had high postprandial serum TG level, out of 64 patients 55 were diabetic. Only 9 patients were not diabetic. In the remaining 36 patients who had normal postprandial S. TG level, 13 were diabetic and 23 were non-diabetic. There was strong association found between diabetes mellitus and high PP4TG levels ( $P < 0.0001$ ) (Table 5).

## DISCUSSION

In this study, 69% patients were aged <55 years, while 75% female and 62% male were aged <55 years. This finding

**Table 1: Age distribution according to gender**

Age	Male	Female	Total
35-45	6	17	23
46-55	27	19	46
56-65	16	5	21
>66	7	3	10
Total	56	44	100

**Table 2: Distribution according to PP4TG and HDL**

PP4TG	Normal HDL	Low HDL	Total
Normal	22	14	36
High	20	44	64
Total	42	58	100

HDL: High-density lipoprotein

**Table 3: Distribution according to WHR and PP4TG**

WHR	Normal PP4TG	High PP4TG	Total
Normal	22	2	24
High	14	62	76
Total	36	64	100

WHR: Waist-hip ratio

**Table 4: Distribution according to BMI and PP4TG**

BMI	Normal PP4TG	High PP4TG	Total
Normal	6	2	8
Overweight	16	24	40
High	14	38	52
Total	36	64	100

BMI: Body mass index

**Table 5: Distribution according to diabetes and PP4TG**

Diabetes	Normal PP4TG	High PP4TG	Total
Absent	23	9	32
Present	13	55	68
Total	36	64	100

shows that middle age patients are more likely to be selected for study like the present study. In Iso *et al.*<sup>9</sup> study, 55% were male and 45% were female, average age was  $55.1 \pm 6.3$  years. In that study, the majority of patients were from middle age group. In our study, 40% of patients were overweight, 52% of patients were obese, according to the National Institute of Health Definition. The mean BMI was 30.08. The mean BMI in normal PP4TG group was 28.90 and high PP4TG group was 30.87, so there is strong correlation found between high BMI and high PP4TG. In Iso *et al.*<sup>9</sup> study, the mean BMI was 28.08. The mean WHR in normal PP4TG group was 0.968 and high PP4TG group was 1.028, so there is strong correlation found between high WHR and high PP4TG. In Couillard *et al.*<sup>10</sup> study, on postprandial TG response in visceral obesity showed that obesity and WHR are associated with impaired postprandial TG clearance. In our study, 64% were diabetic of which 62.5% of male were suffering from diabetes mellitus, whereas 68.18% females were diabetic. The mean fasting blood sugar (FBS) in normal PP4TG group was 80.30 and high PP4TG group was 168.90, so there is strong correlation found between high FBS and high PP4TG. The mean PP2BS in normal PP4TG group was 174.30 and high PP4TG group was 226.46, so their correlation found between high PP2BS and high PP4TG. In Iso *et al.*<sup>9</sup> study, 52.1% patients were diabetic. A study done by Axelsen *et al.*,<sup>11</sup> on postprandial hypertriglyceridemia and Type-2 diabetes showed postprandial lipid intolerance despite having normal fasting TG level and increased risk of macroangiopathy. In this study, out of 100 patients, 64 patients showed serum TG level more than 160 mg% after 4 h of meal. 34 out of 56 male patients (60.7%) and 30 out of 44 females (68.18%) showed postprandial hypertriglyceridemia these data tells that patient having ischemic heart disease, even if they have normal fasting TG levels, they might have impaired postprandial lipid metabolism. The mean PP4TG was 181.47 mg% suggest that there is an association between coronary artery disease and PP4TG levels and the relative risk was 1.75. In Iso *et al.*<sup>9</sup> study, 58% male and 64% female patients showed postprandial hypertriglyceridemia. In Nordestgaard *et al.*<sup>12</sup> study on non-fasting TGs and risk of myocardial infarction, ischemic heart disease and death in men and women showed that non-fasting TG levels independently predict myocardial infarction, ischemic heart disease, and death. In our study 57 patients were hypertension. 32 male patients (57.14%) were hypertensive and 25 female (56.81%) were hypertensive. The mean systolic blood pressure in normal PP4TG group was 129.88, high PP4TG group was 141.84, and the mean diastolic blood pressure in normal PP4TG group was 84.16, and the high PP4TG group was 88.51, so there is strong correlation found between hypertension and high PP4TG. In Kolovou

*et al.*<sup>13</sup> study on postprandial lipemia in hypertension suggest that patient with hypertension have an exaggerated response and delayed clearance of plasma TG lipase concentration.

## CONCLUSION

There is a positive correction between high WHR, diabetes mellitus and postprandial hypertriglyceridemia in ischemic heart disease patients. Non-fasting TG levels indicate the presence of remnant lipoproteins, which may promote atherosclerosis. Postprandial hypertriglyceridemia may be an independent risk factor for atherosclerosis in ischemic heart disease patients. Evaluation of postprandial TG levels is important during the assessment of ischemic heart disease patients.

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# Organophosphate Poisoning Predicting the Need for Mechanical Ventilator Support

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## Abstract

**Background:** The easy availability and lack of legal strictures have made organophosphorus compound poisoning the deadly bane for the people of the lower socioeconomic strata, i.e., farmers and laborers. This study was conducted to predict the need for ventilator support in organophosphate poisoning and to identify the factors which help in predicting the need for ventilatory support in organophosphorus compound poisoning.

**Materials and Methods:** A total of 100 consecutive patients presenting with organophosphate poisoning admitted to New Civil Hospital, Surat, from September 2014 to October 2015 are studied. A provisional diagnosis of organophosphorus poisoning was made on the basis of a definite history of organophosphorus poisoning by patient or attendants and examination of the container when available. The diagnosis was further substantiated by typical clinical features (hypersalivation, miosis, and fasciculations) and characteristic odor of stomach wash or vomitus and serum cholinesterase level and analyzed using proper statistical test, i.e., Chi-square test.

**Results:** With regard to grading of poisoning and its correlation of symptoms, 67% were of mild grade, 19% were of moderate grade, and 14% were of severe grade. Respiratory failure was the most common complication which may develop with 24 h after exposure. Only 2 out of 67 patients required ventilatory support with mild poisoning, 4 out of 19 patients with moderate poisoning required ventilator support, and 8 out of 14 patients with severe poisoning required ventilator support with significant ( $P > 0.001$ ) association between severity by grading system and need of ventilation.

**Conclusions:** A grading system is developed to assess the patients at the time of admission so as to grade the severity of poisoning and deciding requirement of assisted ventilation and thereafter intensive care unit stay is to be decided. Ventilators are boon to patients with respiratory failure due to poisoning and decrease the mortality secondary to organophosphorus related respiratory failure.

**Key words:** Fasciculations, Mechanical ventilation, Organophosphate

## INTRODUCTION

India is predominantly an agricultural country hence pesticides and insecticides are used abundantly during cultivation. Thus, it being natural to have access to this chemical substance by human beings, the contact or usage of these compound may either be accidental or suicidal and rarely homicidal.<sup>1-9</sup>

Organophosphate poisoning is an ever increasing and troublesome situation in the developing countries and is a major health care challenge in the 21<sup>st</sup> century. Hence, this study has been conducted with special interest to ventilatory support in the treatment of organophosphorus poisoning, since the leading cause of death in organophosphorus poisoning is respiratory failure.<sup>10-21</sup>

Organophosphates are extremely toxic chemicals which present with a myriad of clinical problems all of which lead to difficulties in determining management. The organophosphates are an extremely toxic group of compounds which are rapidly absorbed by the dermal and oral routes. The following significant exposure symptoms of toxicity generally occur within 4 h.<sup>22-26</sup>

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The exception to this is extremely lipid soluble organophosphate (e.g., fenthion and dichlofenthion) which are rapidly taken into fat stores and subsequently slowly and intermittently released and metabolized to more active compounds. In this situation, the symptoms of toxicity may not occur for up to 48 h. The easy availability and lack of legal strictures have made organophosphorus compound poisoning the deadly bane for the people of the lower socioeconomic strata, i.e., farmers and laborers.<sup>27-41</sup>

### Purpose

1. To predict the need for ventilator support in organophosphate poisoning
2. To study the clinical profile of organophosphate compound poisoning
3. To identify the factors which help in predicting the need for ventilatory support in organophosphorous compound poisoning.

## MATERIALS AND METHODS

A total of 100 consecutive patients presenting with organophosphate poisoning admitted to New Civil Hospital, Surat, from September 2014 to October 2015 are studied.

### Sample Size

Hospital statistics has shown that about 130 cases of organophosphate poisoning in a year are admitted to New Civil Hospital, Surat. Hence, all the cases with inclusive and exclusive criteria are selected during September 2014 to October 2015.

### Method of Collection of Data

About 100 consecutive patients presenting with organophosphate poisoning were included in the study.

### Inclusion Criteria

A provisional diagnosis of organophosphorus poisoning was made on the basis of a definite history of organophosphorus poisoning by patient or attendants. This was substantiated by examination of the container (which was available in over 50% cases), when available. The diagnosis was further substantiated by typical clinical features (hypersalivation, miosis, and fasciculations) and characteristic odor of stomach wash or vomitus and serum cholinesterase level.

### Exclusion Criteria

The patients with a concomitant illness or condition likely to accentuate the respiratory failure due to organophosphorus poisoning were excluded from the study. These included:

1. Patients with double poisoning with opioids, diazepam, and barbiturates

2. Patients with chronic lung disease, e.g., chronic obstructive pulmonary disease, extensive pulmonary tuberculosis, interstitial lung disease bronchiectasis, and bronchial asthma
3. Patients with chronic cardiac disease
4. Patients with known neuromuscular disease such as myasthenia gravis or muscular dystrophy.

### Statistics

Data will be analyzed by,

1. Diagrammatic presentation
2. Mean  $\pm$  standard deviation
3. Using proper statistical test, i.e., Chi-square test.

### Research Hypothesis

The ventilator support in organophosphorus poisoning patients decreases the mortality secondary to organophosphorus related respiratory failure.

## RESULTS

Of 60 patients with Glasgow Coma (GC) Scale between 11 and 15, 0 required assisted ventilation, 32 patients with GC Scale between 7, and 10.6 (19%) required ventilation, whereas 8 patients with GC Scale between 3 and 6, 8 (100%) required assisted ventilation. This association between GC scale and need of ventilation is highly sensitive with  $P = 0.0000001$  (Figure 1 and Table 1).

Of 28 patients with pinpoint pupils at admissions 13(46%) required ventilations (Table 2). This associations between pupil size and need of ventilation is highly significant ( $p$  value 0.0000001).

Patients with high fasciculation score required assisted ventilation more frequently when compared to patients with absent or only localized fasciculations (Table 3).

Most of the cases categorized for grading, 67% were in mild category, 19% in moderate, and 14% in severe poisoning at the time of admission (Table 4). Among 14 patients of poisoning which graded severe, 8 patients (57.14%) were intubated and put on ventilator. From 19 patients of moderate and 67 patients of mild poisoning, 4 (21.05%) patients and 2 (2.98%) patients required ventilation, respectively. Hence, the association between severe grade of poisoning and need of ventilation is highly significant with  $P = 0.0000461$ .

## DISCUSSION

Of the various agents used for suicidal attempts in India, organophosphorus compound forms a significant group.

**Table 1: Effect of sensorium on need for ventilatory support**

GC scale	Number of patients ventilated	Number of patients non-ventilated	Number of patients
3-6	8	0	8
7-10	6	26	32
11-15	0	60	60
		8	

$P=0.0000001$ , highly significant, Chi-square test - 59.51. GC scale: Glasgow Coma scale

**Table 2: Effect of pupillary size on need for ventilatory support**

Pupil	Number of patients ventilated	Number of patients non-ventilated	Number of patients
Pin point	13	15	28
<1 mm	1	28	29
2-3 mm	0	40	40
4 mm	0	3	3

$P=0.00000018$ , highly significant, Chi-square test - 34.14.

**Table 3: Presence of fasciculations and need for ventilatory support**

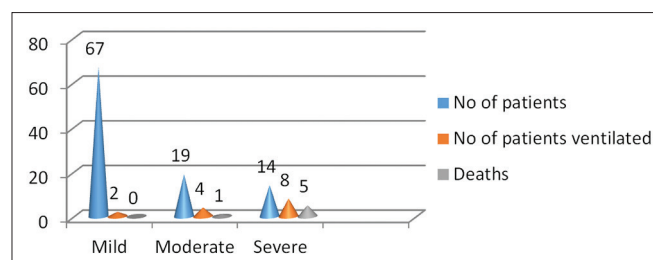
Fasciculation	Number of patients ventilated	Number of patients non-ventilated	Number of patients
<2+	0	45	45
2-4+	1	35	36
>4+	13	6	19

$P<0.000001$ , highly significant, Chi-square - 57.83

**Table 4: Requirement of ventilatory support in relation to severity of organophosphorus poisoning**

Grading	Non-ventilated	Ventilated	Total
Mild	65	2	67
Moderate	15	4	19
Severe	06	8	14

$P=0.0000461$ , highly significant, Chi-square test - 1.53

**Figure 1: Requirement of ventilator support in relation to severity of organophosphorus poisoning**

This is peculiar to developing countries like India, in developed countries 80% of suicidal poisoning result from intake of sedatives, antidepressants, and other related agents.<sup>38</sup>

Organophosphorus insecticides are highly toxic to humans. Poisoning due to organophosphorus insecticides is steadily increasing in India. These pesticides are preferred for the purpose of suicide due to their easy availability and potent toxicity.

In a series of 312 cases of acute poisoning reported in Singh *et al.* (1984),<sup>46</sup> organophosphorus compounds were recorded as the poisons used for suicidal purpose in 19.23% of cases. Diazinon seems to be the choice in the majority of cases. Goel *et al.* reported 28% of cases of poisoning over 1½ years period resulted from organophosphorus compound.

Our study shows, 56% of cases of organophosphorus poisoning over span of 20 months in this institution which is referral hospital. The difference may be due to the fact that their study population was different from this study also in different in part of the country.

The peak incidence of suicide as reported by Quinby (1968),<sup>40</sup> Balani *et al.* (1968),<sup>41</sup> Gupta and Patel (1965)<sup>42</sup> was in the third decade of life followed by second decade, whereas incidences described by Vishwanathan and Shrinivasan 1962<sup>43</sup> was similar in both decades. Goel *et al.*<sup>44</sup> reported an incidence of 86.4% of cases including second and third decade. In our study, peak incidence of 73% was in 15-35 years age group. The age group 15-35 years is the most critical period, this is when one likely to phase various problems that may lead to psychological stress and ultimately force a person to take drastic steps to end his life by consuming available poisons.

In this study, female dominate to attempt suicide than males. Vishwanathan and Shrinivasan (1962)<sup>43</sup> reported higher number of suicidal cases among female than males. While, Mutalik *et al.* (1962),<sup>45</sup> Gupta and Patel (1968),<sup>42</sup> Balani *et al.* (1968),<sup>41</sup> and Goel *et al.* (1998)<sup>44</sup> reported higher number of males patients.

The female predominance in the study indicates the easier accessibility of organophosphorus compound to them. The majority of cases were in the age group 15-35 years.

The organophosphorus compound was consumed by 96% of case with intention to commit suicide. Occupational exposure was the source in 2%. Goel *et al.*<sup>44</sup> reported similar findings. Whereas, Quinby (1964)<sup>40</sup> reported that 50% of cases resulted from occupational exposure and 4.6% were of intentional suicide.

Among the organophosphorus compounds, diazinon was the choice in the study reported by Singh *et al.*<sup>46</sup> Tick - 20 (2% fenitrothion) was of choice in the study reported

by Agarwal monocrotophos and organophosphorus compound of choice in study by Goel *et al.* In our study, dimethoate was commonly used (34%).

Ventilatory support requirement specially with dimethoate was more in the present study which is similar to Goel *et al.*<sup>44</sup> study.

The fact that 96% cases were suicidal in our study group, it is in sharp contrast to figures reported from developed nations like Japan, where accidental occupational exposure forms bulk of organophosphorus cases.<sup>39</sup> The proportion of organophosphorus poisoning resulting from occupational exposure may be misreported to be low from developing world because such cases may not always seek medical attention, as a result of mild atypical symptomatology.<sup>47</sup>

Clinically vomiting, pain abdomen, altered sensorium, hypersalivation, and breathlessness were common symptoms in this study. One patient had convulsions in our study compared to Goel *et al.*<sup>44</sup> who reported 6.7%.

Clinical science such as miosis, pungent odor, tachycardia, signs of respiratory insufficiency, fasciculations, and altered sensorium was common in our study. Mutalik *et al.* (1962),<sup>45</sup> Balani *et al.* (1968),<sup>41</sup> Gupta and Patel (1968),<sup>42</sup> Agarwal (1991).<sup>39</sup> Goel *et al.*, 1998,<sup>44</sup> also observed similar clinical scenario in their study.

With regard to grading of poisoning and its correlation of symptoms, 67% were of mild grade, 19% were of moderate grade, and 14% were of severe grade.

Respiratory failure was the most common complication which may develop with 24 h after exposure.<sup>9-11,39,46-50</sup> Early onset of respiratory failure is due to cholinergic over activity, whereas late onset respiratory failure has been attributed to respiratory infections.

Of the 14 patients who required ventilator support, 9 (64.29%) required it within first 24 h after exposure to organophosphorus compound.

Tsao *et al.* (1990)<sup>11</sup> reported 40.2% of patients developed respiratory failure of which 80.2% developed during 24 h after exposure.

Relationship between delay in institution of specific treatment and survival was found to be insignificant by Mutalik *et al.*<sup>45</sup> but Goel *et al.*<sup>44</sup> showed significant relationship between delay in treatment and requirement of ventilator support. This study also shows that 23 patients have time lag of 3 or more hours for initial treatment of which 4 (17%) required ventilator support.

Only 2 of 67 patients required ventilatory support with mild poisoning, 4 of 19 patients with moderate poisoning required ventilator support, and 8 of 14 patients with severe poisoning required ventilator support with a significant association between severity by grading system and need of ventilation.

## CONCLUSION

Organophosphorus compounds are commonly used agents for suicidal purpose because of their easy availability.

Females are more vulnerable due to a lot of domestic and marital problems. These compounds are reversible inhibitors of cholinesterase.

The common mode of death is due to respiratory failure which requires assist ventilation; other symptoms commonly involved are cardiac and central nervous system.

A grading system is developed to assess the patients at the time of admission so as to grade the severity of poisoning and deciding requirement of assisted ventilation and thereafter intensive care unit stay is to be decided.

Ventilators are boon to patients with respiratory failure due to poisoning and decrease the mortality secondary to organophosphorus related respiratory failure.

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# Role of Alvarado Score in Diagnosis and Management of Acute Appendicitis

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## Abstract

**Background:** Appendicitis is one of the most common conditions responsible for the admission of patients to hospital for surgical treatment.

**Materials and Methods:** This study is prospective cohort study. The patients with classical symptoms and sign of acute appendicitis were admitted to the surgical ward were subjected to investigations including hemoglobin, total leukocytes count (TLC) and differential leukocytic count, blood sugar, X-ray abdomen and ultrasound of abdomen. The patients were evaluated according to Alvarado score. The study was conducted in 385 patients over 1-year period.

**Results:** A total of 385 patients with appendicitis were evaluated (30.39%) patients were of Alvarado score 6 or more. The majority of cases 315 (81.82%) out of 385 treat conservatively and 70 (18.18%) patients were operated. Patients with Alvarado score >7, 13 (3.37%) had positive operative findings and 11 (2.85%) had positive histopathological examination.

**Conclusions:** In this study, we found that clinical score is a simple, rapid, and noninvasive method to early diagnosis of appendicitis. TLC are inflammatory marker are also useful in the early diagnosis of acute appendicitis. Ultrasound abdomen is also useful to confirm the diagnosis. The majority of our patients presented early disease. Because of these negative appendectomy rate are decreasing and morbidity period is also decreasing pre- or post-appendectomy. In our study, we concluded that timely intervention reduces the negative appendectomy and reduce the length of morbidity.

**Key words:** Alvarado score, Appendectomy, Appendicitis

## INTRODUCTION

Appendicitis is one of the most common conditions responsible for the admission of patients to hospital for surgical treatment. Appendicitis is generally regarded as an inflammatory condition, reflected by the suffix to its name. However, it is apparently not influenced by the antibiotics.<sup>1</sup>

In acute appendicitis, it is not possible to have definitive diagnosis by the gold standard (histopathology) preoperatively; we would like a simple test like Alvarado scoring system which depends on the presence and absence of certain variables. Alvarado scoring system was identified

as a useful clinical tool because it is readily available, extremely affordable and relatively accurate. Delay in diagnosis will lead to complication, which increases morbidity, whereas overzealous diagnosis may lead to negative Appendectomy rate<sup>1-3</sup> due to overzealous diagnosis.<sup>4</sup>

This study involves to correlate the appendicitis between clinically diagnosed and histopathologically examined specimen and role of ultrasound in the early diagnosis of appendicitis and to exclude negative appendectomy, in 385 patients admitted to surgical ward Sanjay Gandhi Memorial Hospital associated Shyam Shah Medical College, Rewa for 1-year.

## MATERIALS AND METHODS

This study “role of Alvarado score in diagnosis and management of acute appendicitis” was carried out in 385 patients of appendicitis admitted to surgical wards of Sanjay Gandhi Memorial Hospital, associated with Shyam

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Shah Medical College, Rewa, Madhya Pradesh, during the period of 1-year.

On admission, the particulars of the patients regarding age, sex, occupation, and residence were recorded, presenting complaint, past illness, and associated illness were recorded. Patients were evaluated according to Alvarado score as follows:

Alvarado score	
Symptoms	
Migratory RIF pain	1
Anorexia	1
Nausea/vomiting	1
Signs	
RIF tenderness	2
Rebound tenderness	1
Increase in temperature	1
Lab findings	
Leucocytosis	2
Shift to the left	1
Total	10

RIF: Right iliac fossa

Scoring system	
1-4	Appendicitis unlikely
5-6	Appendicitis possible
7-8	Appendicitis probable
9-10	Appendicitis definitive

### USG Criteria of Acute Appendicitis

Acute appendicitis was confirmed by the presence of noncompressible aperistaltic blind end tubular structure, i.e., appendix - diameter >6 mm, wall thickness >3 mm, complex mass (echo poor, asymmetric) irregular asymmetrical, loss of contour, free fluid, local adynamic ileus, probe tenderness over RIF.

Patients which score 7 or >7 were subjected to surgery. Patients with acute appendicitis were operated in emergency or elective appendectomy was offered to those patients who responded to conservative treatment. Surgery was done under spinal anesthesia. Postoperatively patients were kept nil orally, till bowel sounds returned, parenteral fluid, electrolytes, antibiotics, and analgesics were continued. Cases were watched for any post-operative complications were treated wherever needed. Postoperatively sutures were removed on 7-9 days, and the patients were discharged and followed up in SOPD.

### OBSERVATIONS (TABLES 1-9)

All the data was recorded and following observations were made regarding the investigations done and signs and symptoms observed.

## DISCUSSION

In this study, it was concluded to evaluate Alvarado scoring system to diagnosis of appendicitis and its correlation by total leukocytes count (TLC), ultrasound, and histopathology in our set up.<sup>2</sup>

Clinical scoring system is a good supporting tool for diagnosis for appendicitis because it is simple, easy to use and noninvasive to use clinical routine practice. There was no special equipment required.<sup>2</sup>

In this study, the patients who admitted for elective appendectomy as a routine admission Alvarado score of

**Table 1: Incidence of various signs**

Signs	Number of cases (%)
Tenderness in RIF	349 (90.65)
Rebound tenderness	120 (31.17)
Muscle guarding	107 (27.79)
Rigidity	50 (12.99)
Lump in RIF	76 (19.74)
Abdominal distension	37 (9.61)
Bowel sounds	
Normal	318 (82.60)
Absent	07 (1.82)
Sluggish	38 (9.87)
Increased	22 (5.71)
Per rectal digital examination	
Normal	320 (83.12)
Tenderness in rectum	51 (13.25)
Bulging mass	14 (3.64)

RIF: Right iliac fossa

**Table 2: Hematological investigations**

TLC	Polymorph (%)		Total
	>75	<75	
>10,000	100 (51.81)	93 (48.19)	193 (50.13)
<10,000	90 (46.88)	102 (53.13)	192 (49.87)
Total	190 (49.35)	195 (50.65)	385 (100.00)

TLC: Total leukocytes count

**Table 3: Distribution of cases according to Alvarado scores**

Alvarado score	n (%)		
	Male	Female	Total
1	-	-	-
2	01 (100.0)	0	01
3	-	-	-
4	40 (58.82)	28 (41.18)	68 (17.66)
5	58 (56.86)	44 (43.14)	102 (26.49)
6	62 (52.99)	55 (47.01)	117 (30.39)
7	25 (69.44)	11 (30.56)	36 (9.35)
8	15 (57.69)	11 (42.31)	26 (6.75)
9	18 (66.67)	09 (33.33)	27 (7.01)
10	06 (75.00)	02 (25.00)	08 (2.08)
Total	225 (58.44)	160 (41.56)	385 (100.00)

**Table 4: Distribution of cases with differential leukocyte count according to Alvarado scores**

Scores groups	n (%)		Total
	TLC		
	(>10,000)	(<10,000)	
Alvarado score			
<7	185 (57.10)	139 (42.90)	324 (84.16)
>7	07 (11.48)	54 (88.52)	61 (15.84)
Total	192 (49.87)	193 (50.13)	385 (100.0)

TLC: Total leukocyte count

**Table 5: Distribution of cases with differential neutrophils count according to Alvarado score**

Scores groups	n (%)		Total
	Neutrophills		
	>75	<75	
Alvarado score			
<7	170 (52.47)	154 (47.53)	324 (84.16)
>7	25 (40.98)	36 (59.02)	61 (15.84)
Total	195 (50.65)	190 (49.35)	385 (100.0)

**Table 6: Incidence of different types of appendicular lesions**

Type of appendicular lesion	Number of cases (%)
Acute appendicitis	250 (64.93)
Appendicular lump	66 (17.14)
Recurrent appendicitis	56 (14.54)
Appendicular perforation peritonitis	06 (1.55)
Appendicular abscess	07 (1.81)
Total	385 (100.00)

these patients calculated according to symptoms and sign present during their acute attack of appendicitis.<sup>7</sup>

In this study, we observed the operative findings of patients and classify them into positive and negative. Positive findings mean presence of transmural inflammation or pus in the lumen of appendix. A negative finding means one which performed a clinical diagnosis of acute appendicitis but when the appendix is found to be normal on histopathological examination. This includes histologically normal appendix with or without the presence of fecolith or parasite in the lumen.<sup>5</sup>

We observed incidence of appendicular lesions was 385 (4.28%) out of all surgical admissions (8562). Ashley<sup>1</sup> also found incidence of appendicitis is (12%) in subpopulation.

We observed maximum incidence of appendicitis in the age group 20-40 years (50.64%). Ashley<sup>1</sup> also found incidence of appendicitis more in the young adults with a

**Table 7: Distribution of cases according to management**

Management	Number of cases (%)
Conservative	315 (81.82)
Operative	70 (18.18)
Total	385 (100.0)

**Table 8: Distribution of management according to various appendicular lesion**

Type of appendicular lesion	Number of cases	Management	
		Conservative (%)	Operative (%)
Acute appendicitis	250	234 (93.6)	16 (6.4)
Recurrent appendicitis	50	07 (14.00)	43 (86.00)
Appendicular lump	66	65 (98.48)	01 (1.52)
Appendicular perforation peritonitis	06	00 (0.00)	06 (100.00)
Appendicular Abscess	13	09 (69.23)	04 (30.77)
Total	385	315 (81.82)	70 (18.18)

**Table 9: Distribution of operated cases according to various parameters, operative findings and histopathological report**

Parameters	n (%)			
	Operative findings		Histopathological reports	
	Positive	Negative	Positive	Negative
Alvarado score				
>7	13 (3.37)	311 (80.77)	11 (2.85)	313 (80.77)
<7	58 (15.06)	03 (0.77)	58 (15.06)	03 (0.77)
TLC				
>10,000	11 (2.85)	184 (47.79)	11 (2.85)	169 (43.89)
<10,000	59 (15.32)	134 (34.80)	58 (15.32)	105 (27.27)
Polymorph				
>75	28 (7.27)	158 (41.03)	28 (7.27)	158 (41.03)
<75	42 (10.90)	157 (40.77)	41 (10.90)	159 (41.29)

TLC: Total leukocyte count

peak age of appendicitis is 18 years of age. Chamisa<sup>5</sup> also found majority of patients incidence of appendicitis in the second decades.<sup>1,5</sup>

In our study, we observed the most common clinical sign were tenderness in RIF (90.65%) and rebound tenderness (31.17%). This result comparable with the Dipak (2006) when the most common sign is tenderness in RIF followed by rebound tenderness. The other retrospective analysis by Chmisa found the most common sign is abdominal tenderness.<sup>5,7</sup>

In our study, Alvarado score was found to be the most important diagnostic parameter of appendicitis.<sup>2</sup>

We observed that TLC >10,000 in (50.13%) patients and neutrophils >75 in (48.13%) patients.

We observed that TLC >10,000 with Alvarado score >7 was found in 11.48% while TLC > 10,000 with Alvarado score <7 was found in 57.10%. Normal WBC Count in appendicitis in the present study was 50.13%, i.e., TLC alone is not a positive indicator to rule out appendicitis. Ire Teicher *et al.* reported that in nondifferentiating factors of appendicitis one of the white blood cell count between 10,000 and 13,000 were found equally in both groups, i.e., appendicitis and nonappendicitis.<sup>3</sup>

It is obvious that when the clinical sign of appendicitis shows the Alvarado score more than 6, the findings are confirmed by leukocytosis. Leukocytosis is present in the inflammatory changes, even though clinically Alvarado score may show a lower count. Thus, in this study, Alvarado score alone only appears to be a good indicator in predicting appendicitis but along with TLC, polymorph count and it become more reliable.<sup>7</sup>

Clinical sign symptoms and TLC were the important hallmark of our study. Pain and tenderness in RIF and raised TLC, Alvarado score higher than 6 formed the quick diagnostic tools of acute appendicitis. Fever, vomiting, loose motion, shifting of pain, rigidity, and raised TLC are present only in few cases of acute appendicitis hence their absence cannot rule out of the inflammatory pathology.<sup>7</sup>

In our study, we observed that positive ultrasound findings of 54 (93.10%) out of 58 had undergone surgery, while only 4 (6.90%) patient had conservative treatment. Our study shows that ultrasound in appendicular lesion has a high true positive result.

In our study, it is found that Alvarado scoring systems are superior in diagnosis of acute appendicitis.<sup>2,6</sup>

In our study, the majority of appendicitis patients treated conservatively (81.82%) and 70 (18.18%) patients underwent operative intervention.

In this study, we found that clinical score is a simple, rapid, and noninvasive method to early diagnosis of appendicitis. TLC and ultrasound of abdomen are also useful in appendicitis.

Our study was primarily designed to differentiate between appendicitis and other acute abdominal conditions which could be treated conservatively.<sup>3</sup>

In this study, the policy of controlled observation rather than immediate laparotomy for a diagnosis of questionable appendicitis has resulted in decreasing the rate of negative appendectomy. Or decreasing the morbidity as well as mortality.<sup>3</sup>

## CONCLUSIONS

After analyzing, the data following conclusion are drawn as follows:

- Majority of the patients 117 (30.39%) were of Alvarado score 6 and more followed by score between 4 and 6, i.e., 287 (74.0%).
- In the present study with Alvarado score <7, 185 (57.10%) patients out of 324 had TLC >10,000 while 139 (42.90%) patients had TLC <10,000. With Alvarado score >7, 07 (11.48%) patients out of 61 had TLC >10,000 while 54 (88.52%) patients had TLC <10,000. In this study, we observed that 192 (49.87%) patients had TLC >10,000.
- The most common symptom was pain in abdomen 385 (100.0%) and other symptoms migration of pain in lower abdomen in 249 (64.68%), fever 197 (51.17%), nausea/vomiting 186 (48.31%), and anorexia 171 (44.44%).
- The most common sign was tenderness in RIF (90.65%) and next common signs were muscle guarding (27.79%) and rebound tenderness (31.17%).
- Patient with TLC >10,000 also having raised polymorph (>75) in 100 (51.81%) cases, while patients with the TLC <10,000 having polymorph >75 only in 90 (46.88%) cases.
- With Alvarado score <7, 170 (52.47%) patients out of 324 had neutrophils >75%, while 154 (47.53%) patients had neutrophils <75%. With Alvarado score >7, 25 (40.98%) patients out of 61 had neutrophils >75%, while 36 (59.02%) patients had neutrophils <75%. In this study, we observed that 195 (50.65%) patients had total neutrophils >75%.
- Majority of the patients were of acute appendicitis (64.93%) followed by recurrent appendicitis (14.54%), appendicular lump (17.14%), and lowest incidence found in appendicular abscess (1.81%), appendicular perforation peritonitis (1.55%).
- Majority of the patients with having Alvarado score <7 acute appendicitis 238 (95.12%) out of 250 cases. And >7 having only 12 (4.86%) patients out of 250 cases.
- Majority of the patients with having TLC >10,000 acute appendicitis 138 (55.2%) out of 250 cases. And TLC <10,000 of 112 (44.8%) out of 250 cases.
- Majority of patients positive ultrasonography finding, 54 (93.10%) patients out of 58 had undergone surgery, while only 4 (6.90%) patients had conservatively treatment. This study shows that ultrasonography in appendicular lesion has high sensitivity.
- Majority of the cases 315 (81.82%) out of 385 treat conservatively and 70 (18.18%) patients were treated operatively.
- With acute appendicitis, 234 (93.6%) patients out of 250 had conservative management while 16 (6.4%)

patients had operative management. With recurrent appendicitis, 43 (86%) patients out of 50 had operative management, while 7 (14.0%) patients had conservative management, with appendicular lump 65 (98.48%) patients out of 66 had conservative management while only 1 patient was operated, with appendicular perforation all 6 patients were subjected to operative management. With appendicular abscess, 9 (69.23%) patients out of 13 had conservative management; while 4 (30.77%) patients had operative management.

- In this study according to type of operation, out of 70 patients, 43 (61.42%) of the patients were subjected to elective appendectomy, followed by, 16 (22.85%) emergency appendectomy, 6 (8.57%) exploratory laparotomy, 1 (1.43%) laparoscopic appendectomy, 1 (1.43%) I and D.
- In this study according to type of operative incision, 35 of the patients were operated by McBurney's incision, followed by 19 of Lanz incision, 8 of Rutherford Morrison incision, 6 of Midline incision, 1 of paramedian incision and 1 of laparoscopic port site incision.
- In the present study according to position of appendix, 38 (54.28%) of the patients were retrocecal, followed by 15 (21.42%) of pelvis, 7 (10.0%) of subcecal, 5 (7.14%) of preileal, 4 (5.871%) of paracecal.
- In the present study, patients with Alvarado score >7, 13 (3.37%) had positive operative findings and 11 (2.85%) had positive histopathological examination

and patients with TLC >10,000, 11 (2.85%) had positive operative findings and 11 (2.85%) had positive histopathological examination. And polymorph >75, 28 (7.27%) had positive operative findings and 28 (7.27%) had positive histopathological examination.

In this study, we found that clinical score is a simple, rapid and noninvasive method to early diagnosis of appendicitis TLC as inflammatory marker is also useful in the early diagnosis of acute appendicitis, and ultrasound abdomen are also useful to confirm the diagnosis and plan the management.

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# Diagnostic Accuracy of Fine Needle Aspiration Cytology in Thyroid Swelling with Histopathologic Correlation in Vindhya Region, Central India

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## Abstract

**Introduction:** Fine needle aspiration cytology has been shown to simple, safe, cost-effective, and quick to perform the procedure with excellent patients compliance. We evaluate the usefulness of fine needle aspiration cytology (FNAC) as an initial investigation of choice in patients with thyroid swelling.

**Materials and Methods:** This is a prospective study conducted over 2 years from 1 August 2014 to 31 July 2016 included 78 patients. They were subjected to FNAC, and after surgery, all specimens were sent for histopathological examination. Pre-operative FNAC results were compared with the final histopathological report.

**Results:** A total of 78 patients of thyroid swelling were studied, which included 66 female and 12 male patients with M: F of 5.5:1. The most common symptom was diffuse swelling of thyroid (68.4%). Most (36.28%) of the patients were in age group of 31-40. Most commonly diagnosed problem was colloid goiter, i.e. 66.67%. Malignancy found only in 16.67%. The sensitivity of FNAC to diagnose carcinoma in this study was 75%, specificity was 98.38%, and accuracy was 93.58%.

**Conclusion:** FNAC is well-stabilized technique for pre-operative evaluation of thyroid swelling.

**Key words:** Fine needle aspiration cytology - fine needle aspiration cytology, Histopathology, Thyroid swelling

## INTRODUCTION

Neck swelling is the common clinical presentation in surgery outpatient department and it carries significant morbidity. Enlargement of thyroid gland accounts for significant number of cases of neck swelling. Thyroid swelling can be benign as well as malignant. In 1870, Rugu and his associate Joham Vent have the first advocated surgical biopsy as an essential diagnostic tool for thyroid swelling.<sup>1</sup> Fine needle aspiration cytology (FNAC) can be used to rule out malignancy so that we can avoid unnecessary surgery. FNAC has gained worldwide acceptance since last many years, and emerged as the first choice for the

evaluation of thyroid swelling.<sup>2</sup> Fine needle aspiration cytology with a small gauze needle (23-27 gauge) has been shown to be simple, safe, cost-effective, and quick to perform the procedure with excellent patient compliance. Use of small gauze needles has allowed a marked drop in the complication rate associated with large bore or core needle biopsies while maintaining diagnostic accuracy. The prevalence of thyroid swelling ranges from 4% to 10% in adult population and 0.2-1.2%.<sup>3</sup> The majority of clinically diagnosed thyroid swelling are non-neoplastic;<sup>4</sup> only 5-30% are malignant and require surgical treatment.

## Aim

The aim of this study was to determine the accuracy of FNAC of thyroid swelling performed at this institution.

## MATERIALS AND METHODS

This is a prospective study conducted over 2 years from 1 August 2014 to 31 July 2016 included 78 patients. All the

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**Table 1: Incidence of thyroid swelling according to FNAC finding**

FNAC report	Number of patients (%)
Colloid goiter	52 (66.67)
Papillary carcinoma	13 (16.67)
Thyroiditis	11 (14.10)
Thyroglossal cyst	2 (2.56)
Total	78 (100)

FNAC: Fine needle aspiration cytology

**Table 2: Correlation of FNAC finding with histopathological finding**

Diagnosis of FNAC	Number of patient diagnosed by FNAC	Comparison with HPE	
		Correct cytological diagnosis	False cytological diagnosis
Colloid goiter	52	48	4
Papillary cancer	13	12	1
Thyroiditis	11	11	0
Thyroglossal cyst	2	2	0

FNAC: Fine needle aspiration cytology

**Table 3: Efficacy of FNAC in diagnosing of carcinoma with correlation to histopathology**

FNAC result	Histopathology		Total
	+ve for carcinoma	-ve for carcinoma	
+ve for carcinoma	12	1	13
-ve for carcinoma	4	61	65

FNAC: Fine needle aspiration cytology

**Table 4: Data sensitivity, specificity and accuracy of FNAC**

Statistical parameteres	Present study (%)	Bouvet <i>et al.</i> (7)%	Kessle <i>et al.</i> (8)%	Gupta <i>et al.</i> (9)%
Sensitivity	75	93.5	79	80
Specificity	98.38	75	98.5	86.6
Accuracy	93.58	79.6	87	84

patients presented with thyroid swelling were evaluated in detail including age, sex, residence, duration of illness, any symptoms suggestive of hypothyroidism or hyperthyroidism and examined clinically after through history taking. They were subjected to FNAC and only those patients (all age group and both sex) who were admitted in surgical wards of SGMH REWA, and operated for thyroid swelling were included in this study. After surgery, all specimens were sent for histopathological examination. Pre-operative FNAC result was compared with the final histopathological report.

## RESULTS AND DISCUSSION

A total of 78 patients of thyroid swelling were studied, which included 66 female and 12 male patients with M: F of 5.5:1. Hirachand *et al.*<sup>5</sup> showed m: f was 12.3:1.

The most common symptom was diffuse swelling of thyroid (68.4%), followed by pain in thyroid region in 18.6%. Gole *et al.*<sup>6</sup> also showed swelling in thyroid region is the most common complaint.

Most (36.28%) of the patients were in age group of 31-40, followed by 26.4% were in 21-30 years.

In this study, the most common (66.67%) disorder was colloid goiter, followed by thyroiditis in 22.51% (Table 1).

Among 78 cases of thyroid swelling 73 cases showed a positive correlation between FNAC and histopathological examination. Out of 52 cases of colloid goiter, 48 cases proved correct on histopathological examination but 4 cases came out as papillary carcinoma, and out of 13 cases of papillary carcinoma 12 cases proved correct and 1 case proved as colloid goiter (Table 2).

According to Table 3, true positive cases were 12, false positive 1, false negative 4 and 61 true negative cases. Using this data sensitivity, specificity and accuracy of FNAC in diagnosing thyroid carcinoma is 75%, 98.38% and 93.58% respectively. (Table 4). Similar results were obtained by different authors as well.<sup>7-9</sup>

## CONCLUSION

FNAC is regarded as an initial investigation of choice for the evaluation of thyroid swelling. It is safe, simple, and cost-effective and free from complication in the expert hand. FNAC with its very high specificity, and diagnostic accuracy, approaching 100% can help to rule out malignancy in most of the thyroid swelling and prevent unnecessary surgery. Currently, pre-operative FNA replacing the use of intraoperative frozen section pathologic analysis.

For palpable nodule FNAC may be performed without image guidance, however, ultrasound guidance may be used for FNAC for the palpable nodule, especially heterogeneous lesion. Ultrasound guidance is recommended for nonpalpable, posteriorly located, or cystic nodule and results in lower rate of nondiagnostic cytology and sampling error.

Sometime FNAC may be inconclusive, in that case, repeat FNAC using ultrasound guidance is indicated and yields diagnostic cytology in 50-75% of cases.<sup>10</sup>

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# Evaluation of Abnormalities of Thyroid Gland by High Resolution Ultrasound and Color Doppler Imaging along with Cytological Correlation

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## Abstract

**Background:** Thyroid lesions are a common finding in the general population, esp. in iodine deficiency areas such as in our country. Thyroid disorders like thyroid neoplasm still pose a major problem in both developing and developed countries. Nodular abnormality of thyroid represents a significant problem worldwide, the incidence of nodular thyroid disease is on the rise owing to the association of childhood irradiation with increased incidence of both thyroid nodularity and carcinoma. In western countries approximately 5% and in iodine-deficient countries approximately 25% of the general populations have thyroid nodules. Although most of them are benign, 5-10% was malignant.

**Materials and Methods:** Random selection of patient of all age groups from various OPDs will be done. Patients referred to us having a palpable thyroid mass or neck swelling or presenting with clinical symptoms suggesting thyroid dysfunction, regardless of age, and sex will be included in the study.

**Results:** This study highlight the usefulness of ultrasonography in the evaluation of the palpable thyroid masses as an adjunct to clinical examination. Ultrasound has added advantage of being safe, non-invasive, rapid. Reliable, acceptable economical and probable imaging modality without hazard of radiation. It can also guide interventional procedures like cyst aspiration and fine needle biopsy. It has also capability to detect small non-palpable thyroid masses (<1 cm in diameter).

**Conclusion:** Ultrasonography is 100% effective in diagnosing a thyroid lesion whether solid. Cystic or mixed. It can help to differentiate a malignant lesion from benign masses, with some limitation. Hence, it can be used as a valuable adjunct to clinical examination and should be offered to all patients presenting with palpable thyroid masses.

**Key words:** Color Doppler, Cytology, Imaging, Thyroid gland, Ultrasound

## INTRODUCTION

Thyroid lesions are a common finding in the general population, esp. in iodine deficiency areas such as in our country. Thyroid disorders like thyroid neoplasm still pose a major problem in both developing and developed countries. Nodular abnormality of thyroid represents a significant problem worldwide, the incidence of nodular thyroid disease

is on the rise owing to the association of childhood irradiation with increased incidence of both thyroid nodularity and carcinoma. In western countries approximately 5% and in iodine-deficient countries approximately 25% of the general populations have thyroid nodules. Although most of them are benign, 5-10% was malignant.

Sonography has become the method that is most commonly employed. The ultrasound examination of the thyroid should always include the entire neck, looking for abnormal lymph nodes, enlarged parathyroid glands, and abnormal masses. Both lobes must be scanned individually in the transverse and longitudinal planes.<sup>1</sup> Its use has resulted in early and accurate detection of various thyroid disorders. This is of immense help in timely management and prevention of complications.

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Now sonography has largely replaced it for the majority of the patient, who require a graphic representation of the regional anatomy because of its higher resolution, superior correlation of true thyroid dimensions with the image, smaller expense, greater simplicity, and lack of need for radioisotope administration.

Color Doppler sonography is used in thyroid vascular study. Dynamic information such as velocity and direction of blood flow as well as degree of vascularity of organ can be revealed by color Doppler studies. Doppler (color and power) evaluation will be done for a good diagnosis because the thyroid is a highly vascular organ, and the vascularization changes during pathological diffuse or nodular processes.<sup>2</sup> The risk of malignancy in a euthyroid patient with a solitary thyroid nodule is estimated to be 5-10% with a range of 3.4-29%.<sup>3-8</sup>

Ultrasound vascular study is a noninvasive and low-cost method and is very reliable in the differential diagnosis of cold thyroid nodule; the best ultrasonographic modality is power Doppler. The majority of cold nodule will demonstrate a peripheral rim of color flow and no internal color flow with color Doppler sonography. A large number of hot nodules will demonstrate internal color flow. The vascular network of the thyroid nodules will distinguish the rare malignant nodules from the high amount of benign ones.<sup>9</sup>

The lymph nodes number and location will be evaluated by screening all the compartments of the anterior and lateral cervical region, along with their diameters and ratio, their shape, structure, and echogenicity.<sup>10</sup> Pathological lymph nodes can be inflammatory or metastatic, and they display some characteristic features.<sup>11,12</sup>

Fine needle aspiration cytology (FNAC) is inexpensive and easy to perform and widely available and will be done as an initial investigation for a thyroid nodule. Ultrasound guided FNAC will be done.<sup>10-14</sup>

- Impalpable or poorly palpable nodules (<2 cm)
- Non-diagnostic or failed previous conventional FNAC.

### Aims and Objectives

1. To study a common thyroid disorder in our setup.
2. Evaluating the accuracy of ultrasound in diagnosing thyroid disorders.
3. To evaluating the important sonological parameters in various thyroid disease.
4. To differentiate between solid, cystic and mixed nodule.
5. To differentiate between benign and malignant thyroid lesions.
6. To evaluate vascular nature of various thyroid lesion using color Doppler.

7. The role of color Doppler in distinguishing benign for malignant thyroid nodules.
8. Comparison of clinical, ultrasound color Doppler and FNAC findings.

## MATERIALS AND METHODS

This is a prospective study of patient presenting with various thyroid anomalies evaluated sonographically and findings correlated with fine needle aspiration cytology and is to be conducted in Department of Radiodiagnosis, N.S.C.B. Medical College, Jabalpur, Madhya Pradesh, India.

### Criteria for Pt. Selection

Patients referred to us having a palpable thyroid mass or neck swelling or presenting with clinical symptoms suggesting thyroid dysfunction, regardless of age and sex will be included in the study.

The most common clinical symptom will be swelling in front of neck, which moves up with deglutition. There will be systemic symptoms, such as pain and fever in thyroiditis weight loss and palpitation in hyperthyroidism, weight gain and hoarseness of voice in hypothyroidism and rapid increase in size with weight loss in malignancies. In nodular goiter patients will be usually euthyroid. The nodules will be palpable and sometimes visible.

Technical consideration:

1. Color Doppler ultrasound unit
  - a. Siemens-Sonoline 0-50
  - b. Logic 3 Expert<sup>2</sup> Ay 15 CUK-GE
2. High-frequency linear array ultrasound transducer with a range 8, 12, 14 MHz.

Linear array transducer will be preferred to sector transducer because of wider near field of view and the capability to combine high-frequency gray scale and color Doppler images.

Doppler settings will be standardized to compare the vascularity of thyroid pathologies among different patients and to ensure intra-individual consistency.

Observations will be recorded in the pro forma and hard copy of imaging mode.

### Technique of Scanning

Examination will be laterally extended to include the region of carotid artery and jugular vein to identify enlarged jugular chain of lymph nodes, superiorly to visualize submandibular adenopathy and inferiorly to define any pathological supraclavicular lymph nodes.

## RESULTS

In this study, the age of the patient ranged from 13 years to 70 years. Table 1 shows the distribution of patients among various age groups. The majority of the patients were in the age group of 40-50 years. The sex wise distribution of cases with thyroid diseases. Females are more commonly affected than male. Ratio between male and female is 8.32 in our study (Table 1).

The clinical diagnosis in this study, out of 40 cases, 10 (25%) were of goiter, 6 (15%) were of neck swelling, 16 (40%) cases were of colloid goiter, 2 (5%) cases were of hyperthyroidism, 2 (5%) cases were of multinodular goiter, 2 (5%) cases of cystic thyroid nodule, and 1 (2.5%) case of nodular goiter and toxic thyroid nodule (Table 1). The involvement of lobe of thyroid. Out of 40 cases, 22 (55%) cases involved both lobe of thyroid 11 (27.5%) cases involved right lobe and 7 (17.5%) involved left lobe (Table 1). The number of lesion on USG. Out of 40 cases, 16 (40%) were having single lesion, 3 (7.5%) were having two lesion, 7 (17.5%) were having diffusely enlarged gland, and 14 (35%) were having multiple lesion (Table 1). The internal content of lesion, out of 40 cases, 2 (5%) cases were purely cystic, 29 (72.5%) were having mixed solid and cystic component and 9 (22.5%) cases were having mixed solid and cystic with comet tail artifact (Table 1).

The echogenicity of lesion, out of 40 cases, 3 (15%) cases were anechoic lesion, 6 (15%) cases were hyperechoic lesion, and 28 (70%) cases were hypoechoic or mixed (Table 1). The presence of halo around the lesion, out of 40 cases, 1 (2.5%) case shows the presence of thick incomplete halo and 39 (97.5%) cases the halo is absent

**Table 1: Distribution of patients among various age groups**

Variables	Number of cases (%)
Age	
<20	2 (5.0)
20-29	5 (12.5)
30-39	8 (20.0)
40-49	14 (35.0)
50-59	9 (22.5)
60-69	2 (5.0)
Sex	
Male	8 (20.0)
Female	32 (80.0)
Presenting complaints	
Neck swelling	39 (97.5)
Throat pain	1 (2.5)
Clinical diagnosis	
Goiter	10 (25.0)
Neck swelling	6 (15.0)
Colloid goiter	16 (40.0)
Hyperthyroidism	2 (5.0)

(Contd...)

**Table 1: (Continued)**

Variables	Number of cases (%)
Multi nodular goiter	2 (5.0)
Cystic thyroid nodule	2 (5.0)
Nodular goiter	1 (2.5)
Toxic thyroid nodule	1 (2.5)
Thyroid lobe	
Both lobe	22 (55.0)
Left lobe	7 (17.5)
Right lobe	11 (27.5)
Number of lesion	
One	16 (40)
Two	3 (7.5)
Diffuse	7 (17.5)
Multiple	14 (35.0)
Internal contents	
Purely cystic	2 (5.0)
Mixed solid and cystic	29 (72.5)
Mixed solid and cystic with comet tail artifact	9 (22.5)
Echogenicity	
Anechoic	3 (7.5)
Hyperechoic	6 (15.0)
Hypoechoic/mixed	28 (70.0)
Halo	
Thick incomplete halo	1 (2.5)
Absent halo	39 (97.5)
Margin	
Well defined	31 (77.5)
Poorly defined	9 (22.5)
Calcification	
Eggshell	4 (10.0)
Coarse	2 (5.0)
Microcalcification	5 (12.5)
No calcification	29 (72.5)
Lymph node	
Absent	37 (92.5)
Present	3 (7.5)
Color Doppler index	
RI	
<0.75	37 (92.5)
>0.75	3 (7.5)
Power Doppler pattern	
Zero	0 (0.0)
Type I	14 (35.0)
Type II	21 (52.5)
Type III	2 (5.0)
Type IV	3 (7.5)
Sonographic diagnosis	
Thyroiditis	6 (15.0)
Colloid goiter	26 (65.0)
Diffuse hyperplasia of gland	2 (5.0)
Malignant thyroid mass	3 (7.5)
Hemorrhagic cyst	2 (5.0)
Follicular adenoma	1 (2.5)
Cytological findings	
Inflammatory lesion of thyroid	5 (12.5)
Colloid goiter	27 (67.5)
Benign follicular neoplasia	1 (2.5)
Follicular carcinoma	2 (5.0)
Colloid goiter with cystic degeneration	1 (2.5)
Hemorrhagic cyst	1 (2.5)
Papillary carcinoma thyroid	1 (2.5)
Graves' disease	1 (2.5)
Follicular adenoma	1 (2.5)

RI: Resistive index

(Table 1). The margin of lesion, out of 40 cases, 31 (77.5%) cases were having well-defined margins and 9 (22.5%) cases were having poorly defined margin (Table 1). Out of 40 cases, 4 (10%) cases having eggshell calcification, 2 (5%) cases having coarse calcification, 5 (12.5%) cases having microcalcification, and 29 (72.5%) cases calcification is absent (Table 1). Out of 40 cases in 37 (92.5%) cases, there is no involvement of lymph node and 3 (7.5%) cases having involvement of lymph node (Table 1).

Out of 40 cases, 10 (25%) cases were clinically diagnosed as goiter. Out of this 10 cases on USG, 2 (20%) were diagnosed as thyroiditis (6%) were diagnosed as colloid goiter and 1 (10%) case was diagnosed as diffuse hyperplasia of gland and malignant thyroid mass. Out of 40 cases, 6 (15%) cases were clinically diagnosed as neck swelling. Out of this 6 cases on USG, 3 (50%) were diagnosed as thyroiditis 1 case was diagnosed as diffuse hyperplasia of gland 2 (33%) case were diagnosed as malignant thyroid mass. Out of 40 cases, 16 (40%) cases were clinically diagnosed as colloid goiter all of them were diagnosed as colloid goiter on USG. Out of 40 cases, 2 (5%) cases were clinically diagnosed as hyperthyroidism, out of these 2 cases, 1 (50%) case was diagnosed as thyroiditis on USG and 1 (50%) case was diagnosed as colloid goiter on USG. Out of 40 cases, 2 (5%) cases were clinically diagnosed as multinodular goiter which was diagnosed as colloid goiter as on USG. Out of 40 cases, 2 (5%) cases were clinically diagnosed as cystic thyroid nodule which was as diagnosed as hemorrhagic cyst on USG. Out of 40 cases, 1 (2.5%) case was clinically diagnosed as nodular goiter which was diagnosed as colloid goiter on USG. Out of 40 cases, 1 case was clinically diagnosed as toxic thyroid nodule which was diagnosed as follicular adenoma on USG (Table 2).

The out of 40 cases in 37 (92.5%) cases having RI value  $<0.75$  and in 3 (7.5%) cases having RI value  $>0.75$  (Table 1).

The patients have Type 2 pattern and 1. Pattern zero corresponding to no flow was not observed in any case. Type 1 pattern in which there is only peripheral flow is seen in 14(35%) nodules. Type 2 pattern having peripheral and central component of flow with peripheral component predominating is seen in 21 (52.5%) patients. Type 3 pattern with central component predominating over peripheral is seen in 2 (5%) patients. Only 3 (7.5%) has type 4 pattern which has only central flow (Table 1). Out of 40 cases, 6 (15%) cases were sonographically diagnosed as thyroiditis, 26 (65%) cases were diagnosed as colloid goiter, 2 (5%) cases were diagnosed as diffuse hyperplasia of gland, 3 (7.5%) cases were diagnosed as malignant thyroid mass, 2 (5%) cases were diagnosed as hemorrhagic cyst, and 1 (2.5%) case was diagnosed as follicular adenoma (Table 1). Out of 40 cases, 5 (12.5%)

cases were cytologically diagnosed as inflammatory lesion of thyroid, 27 (67.5%) cases were diagnosed as colloid goiter, 1 (5%) case was diagnosed as follicular carcinoma, 1 (2.5%) case was diagnosed as colloid goiter with cystic degeneration, 1 (2.5%) case was diagnosed as hemorrhagic cyst, 1 (2.5%) case was diagnosed as papillary carcinoma thyroid, 1 (2.5%) case was diagnosed as Graves' disease, 1 (2.5%) case was diagnosed as follicular adenoma (Table 1).

The comparative study between b mode and FNAC. Out of 40 cases, 6 (15%) cases were diagnosed as thyroiditis on USG, 5 (12.5%) cases were correctly proved by FNAC, and 1 (2.5%) case was diagnosed as follicular adenoma. Out of 40 cases on USG, 2 (5%) cases were diagnosed as diffuse hyperplasia of gland and 1 (2.5%) case was diagnosed as benign follicular neoplasia, and 1 (2.5%) as Graves' disease on FNAC. 3 N(7.5%) cases of malignant thyroid mass were diagnosed on USG, 1 (2.5%) was diagnosed as papillary carcinoma, and 2 (5%) cases were diagnosed as hemorrhagic on USG 1 (2.5%) was correctly proved by FNAC and 1 (2.5%) was diagnosed as colloid goiter with cystic degeneration and 26 (65%) cases were diagnosed as colloid goiter ass of them were correctly proved by FNAC (Table 3).

## DISCUSSION

Thyroid diseases are not uncommon in clinical practice and many of them present itself as thyroid nodule. Clinical biochemical imaging and histological assessment must be closely coordinated in patient with thyroid diseases for confirmation of diagnosis present study have been done in the Department of Radiodiagnosis, N. S. C. B. Medical College, Jabalpur, with title Evaluation of Abnormalities of Thyroid Gland By High Resolution Ultrasound and Color Doppler Imaging Along with Cytological Correlation.

This study included 40 patient of thyroid diseases referred from Department of Surgery, General Medicine, ENT, etc., for ultrasonographic evaluation.

In our study, we have taken 40 cases of the study group. In this study, we found the majority of case between 4<sup>th</sup> and 5<sup>th</sup> decade and above age group. Yokozawa *et al.*<sup>15</sup> reported their experience with 678 patients of benign thyroid nodule by USG and FNAC they reported mean age of  $52.2 \pm 11.9$  years which was higher than what was observed in our study. In present series out of 40 patient, 32 were female and rest 8 were male Solbiati *et al.* in their study of 401 patient found that 71.3% were females and 28% were males. Khurana *et al.*<sup>16</sup> reported their experience with 119 patients out of which 100 (84%) were females and 19 (16%) males.

**Table 2: Clinical diagnosis**

Clinical diagnosis	Sonography diagnosis					
	Thyroiditis	Colloid goiter	Diffuse hyperplasia of gland	Malignant thyroid mass	Hemorrhagic cyst	Follicular adenoma
Goiter	2	6	1	1	0	0
	33.3	23.1	50.0	33.3	0.0	0.0
Neck swelling	3	0	1	2	0	0
	50.0	0.0	50.0	66.7	0.0	0.0
Colloid goiter	0	16	0	0	0	0
	0.0	61.5	0.0	0.0	0.0	0.0
Hyperthyroidism	1	1	0	0	0	0
	16.7	3.8	0.0	0.0	0.0	0.0
Multi nodular goiter	0	2	0	0	0	0
	0.0	7.7	0.0	0.0	0.0	0.0
Cystic thyroid nodule	0	0	0	0	2	0
	0.0	0.0	0.0	0.0	100.0	0.0
Nodular goiter	0	1	0	0	0	0
	0.0	3.8	0.0	0.0	0.0	0.0
Toxic thyroid nodule	0	0	0	0	0	1
	0.0	0.0	0.0	0.0	0.0	100.0

**Table 3: Cytological findings**

Cytological findings	Sonography diagnosis					
	Thyroiditis	Colloid goiter	Diffuse hyperplasia of gland	Malignant thyroid mass	Hemorrhagic cyst	Follicular adenoma
Inflammatory lesion of thyroid	4	1	0	0	0	0
	66.7	3.8	0.0	0.0	0.0	0.0
Colloid goiter	2	25	0	0	0	0
	33.3	96.2	0.0	0.0	0.0	0.0
Benign follicular neoplasia	0	0	1	0	0	0
	0.0	0.0	50.0	0.0	0.0	0.0
Follicular carcinoma	0	0	0	2	0	0
	0.0	0.0	0.0	66.7	0.0	0.0
Colloid goiter with cystic degeneration	0	0	0	0	1	0
	0.0	0.0	0.0	0.0	50.0	0.0
Hemorrhagic cyst	0	0	0	0	1	0
	0.0	0.0	0.0	0.0	50.0	0.0
Papillary carcinoma thyroid	0	0	0	1	0	0
	0.0	0.0	0.0	33.3	0.0	0.0
Graves' disease	0	0	1	0	0	0
	0.0	0	50.0	0.0	0.0	0.0
Follicular adenoma	0	0	0	0	0	1
	0.0	0.0	0.0	0.0	0.0	100.0

In our study, we found the majority of patients 39 of neck swelling and only 1 patient of throat pain. In this study, one thing is coming out major complaints of patient is neck swelling. In our study, out of 40 patients, we found 10 (25%) patients of goiter, 6 (15%) patients of neck swelling, 16 (40%) patients of colloid goiter 2 (5%) patients of hyperthyroidism, 2 (5%) patients of multinodular goiter, 2 (5%) patients of cystic thyroid nodule. and 1-1 patients of nodular goiter and toxic thyroid nodule.

About 26 cases were echographically diagnosed as colloid goiter and 1 case of colloid goiter with cystic degeneration all of them were proved by FNAC. All of them showing

perinodular color flow pattern with RI <0.75. Solbiati *et al.*<sup>17</sup>(1985) found 26(6%) cystic nodules out of 401 cases. All these lesions were goiter and no malignancy was found. Cox *et al.*,<sup>18</sup> in 1,991, found 16 cystic nodules out of 68 patients in which were benign and 1 was malignant. In our study group out of 40 cases, we found 3 (7.5%) cases of anechoic lesion, 6 (15%) cases of hyperechoic lesion, 28 (70%) cases of hypoechoic, and 4 mixed variety of lesion. Takashima *et al.*<sup>19</sup> found that tissue echogenicity is the most useful criteria in making a sonographic diagnosis and that hypoechoic lesion have the highest incidence of malignancy. Papini *et al.*<sup>20</sup> in their study concluded that hypoechoic lesion have a sensitivity of 87%in detecting malignant lesion.

Out of 40 cases, we found only 1 case of thick in complete halo and in rest of 39 cases there is no evidence of halo seen. Summari Vmirk *et al.*<sup>21</sup> in their study of 78 patient found absent halo sign 18/22 carcinoma and in 16/56 benign nodules with a sensitivity of 82% and 71%, respectively.

Out of 40 cases, we found 31 (77.5%) regular margin and in rest of 9 (22.5%) margin are irregular. Andrej Lyshchik *et al.*<sup>22</sup> in their study comprising 103 patients found that the most reliable diagnostic criteria for malignancy is irregular out line with a sensitivity and specificity of 69.6% and 86.4%, respectively.

In our study out of 40 cases, we found eggshell calcification in 3 cases coarse calcification in 2 cases and micro calcification in 5 cases and rest of 30 cases there is absence of calcification. Takashimas *et al.*<sup>19</sup> studied 201 patients with USG to clarify the role of microcalcification in diagnosis of thyroid of tumors and found that sensitivity specificity and positive predictive value of microcalcification was 36%, 93%, 70%, respectively. Papini *et al.*<sup>20</sup> found that at us cancers presented with irregular margins in 77.4% with relative risk of 16.83%.

Out of 40 cases, we found in 37 (97.5%) there is no evidence of lymphadenopathy seen and in rest of 3 (7.5%) cases lymph node present.

On USG diagnosis, out of 40 cases, we found 6 (15%) cases of thyroiditis, 26 (26%) case of colloid goiter, 2 (5%) cases of diffuse hyperplasia of gland, 3 (7.5%) cases of malignant thyroid mass, 2 (5%) cases of hemorrhagic cyst, and 1 case of follicular adenoma.

On cytological examination, out of 40 cases, we found 5 (12.5%) cases of inflammatory lesion of thyroid, 27 cases of colloid goiter, 1 case of benign follicular neoplasia, and 2 case of follicular carcinoma, and case of colloid goiter with cystic degeneration, and 11 case of hemorrhagic cyst and papillary carcinoma Graves' disease and follicular adenoma.

In our study, power Doppler pattern was classified in to 5 sub types. Type zero with no flow at all was not observed in any thyroid nodules. Benign nodules predominantly shows type 2 and type 1 pattern with only 2 nodules showing type 3 pattern. Malignant nodules showed predominantly type 4 pattern. No benign nodule showed type 4 pattern this series shows that type 4 pattern are highly sensitive and specific in detection of malignant thyroid nodule.

De Nicola *et al.*<sup>23</sup> evaluated thyroid nodules and found sensitivity and specificity of type 3 and type 4 pattern in the detection of malignancy were 80% and 89%, respectively.

Miyakawa *et al.*<sup>24</sup> concluded that power Doppler findings have a sensitivity and specificity of 87% and 92%, respectively.

Chammas *et al.*<sup>25</sup> in their study found that power duplex Doppler facilitates screening of thyroid nodules at high risk for malignancy with elevated sensitivity (92.3%) and specificity (88%).

In color Doppler examination, we found 3(7.5%) cases of increased RI value more than .75 and rest of 37 case < 0.75.

Holden found mean RI value of 0.76 in cart in adenoma, and 0.57 in colloid nodule. Cerbone *et al.* RI of greater than 0.75 in 18 of 21 carcinomas and benign nodules. Denicola *et al.* found mean Rivalue carcinomas and 0.60 in benign nodule.

## CONCLUSION

The thyroid lesion was examination by 6-12 MHz electronically focussed linear transducer with patient in supine position with direct contact method.

In our series, age ranges from 13 to 70 years major age group affected in between 40 and 50 years.

Male and female ratio in our study was 1:4 females were found to be affected more than males.

Out of 40 cases, 2 cases were diagnosed as purely cystic, 25 cases were diagnosed as mixed solid and cystic and 9 cases were diagnosed as mixed solid with comet tail artifact which were proved by FNAC examination. Diagnostic accuracy in this series was 100%.

A. Cystic lesion were then grouped under various histologic types depending upon echographic finding in the light of history and physical examination which shows over yield in diagnosis of cystic lesion was 94.4%. 26 cases were echographically diagnosed as colloid goiter and 1 case of colloid goiter with cystic degeneration all of them were proved by FNAC. All of them showing perinodular color flow pattern with RI < 0.75.

2 cases were echographically diagnosed as hemorrhagic cyst 1 of them were proved to be hemorrhagic cyst and 1 case was falsely diagnosed as hemorrhagic cyst due to false interpretation latter on proved to be colloid goiter with cystic degeneration, and malignant lesion. 6 cases were diagnosed as thyroiditis 5 of them found to be correct by FNAC 1 case was turned out to be Graves' disease. All of them showing RI value < 0.75 on color Doppler examination.

Three cases were diagnosed as malignant thyroid mass 1 of them was diagnosed as papillary carcinoma by FNAC showing RI > 0.75 on color Doppler examination and 2 of them was diagnosed as follicular neoplasm by FNAC 4 showing RI > 0.75 1 case were diagnosed as follicular adenoma was correct proved by FNAC with RI value <0.75 on color Doppler examination.

Hypoechoic halo was frequently present in benign lesion than malignant cases were having irregular or incomplete hypoechoic halo. In many cases it was absent. The role of high resolution ultrasonography in the diagnosis of palpable thyroid masses has been assessed in our study and results were encouraging. Sonography attains 100% accuracy in differentiating solid, cystic and complex masses and it provides a diagnostic accuracy in 91% cases in term of tissue characterization.

This study highlights the usefulness of ultrasonography in the evaluation of the palpable thyroid masses as an adjunct to clinical examination. Ultrasound has added advantage of being safe, noninvasive, rapid. Reliable, acceptable economical and probable imaging modality without hazard of radiation. It can also guide interventional procedures like cyst aspiration and fine needle biopsy. It has also capability to detect small non palpable thyroid masses (<1 cm in diameter).

Thus in conclusion ultrasonography is 100% effective in diagnosing a thyroid lesion whether solid. Cystic or mixed.

Although tissue characterization is not always possible by the ultrasound, it can help to differentiate a malignant lesion from benign masses with some limitation. Hence, it can be used as valuable adjunct to clinical examination and should be offered to all patients presenting with palpable thyroid masses.

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# Metastatic Malignant Melanoma: A Case Study

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## Abstract

Malignant melanoma is a cancer of melanocytes usually arising in the skin but can form anywhere that melanocytes exist such as in bowel mucosa, retina, and the leptomeninges. We present a similar case of primary malignant melanoma of left foot, a rare and highly malignant disease with very poor prognosis. It accounts for only 3% of all skin cancers but accounts for 75% of skin cancer-related deaths per year. Radical surgery is the only treatment option. A case of primary malignant melanoma of left foot and ilioinguinal lymph node metastasis was treated by primary wide local excision of primary tumor with post-operative radiotherapy.

**Key words:** Ilioinguinal block dissection, Malignant melanoma, Metastasis, Wide local excision

## INTRODUCTION

Cutaneous malignant melanomas is cancer developing from the pigment-containing cells called melanocytes, occurring most commonly in lower limbs in females and over back in males.<sup>1-3</sup>

Melanomas are the most dangerous type of skin cancer worldwide amounting to only 5% of skin malignancy, but resulting in over 75% of deaths related to skin malignancy. It is the most common cancer in young adult group (20-39 years). It is commonly seen in white skinned Caucasian population which amounts to total 3% of all malignancies. In Indian and Asian population, incidence of malignant melanomas amount to just 0.2-0.5/1,00,000 patient years. Whereas both incidence and mortality are decreasing or leveling off in the younger population, rates are still increasing in the older age groups. The rate of increasing incidence varies geographically with “high incidence regions” like Australia; “moderate incidence regions” like Canada and USA; “low incidence regions” like Scotland and India.<sup>4-5</sup>

Prognosis of melanoma diagnosed earlier is excellent but once it becomes malignant, it becomes very poor with metastasis to brain and visceral organs have very poor prognosis.

## CASE REPORT

A 75-year-old female came with a history of left foot pigmented lesion over medial aspect of ankle of left foot with left inguinal swelling about 10 × 15 cm in size painless in nature. A patient was a known diabetic and hypertensive on medication. The patient was initially planned for excision and biopsy, and treated by wide local excision of pigmented lesion of left foot with split thickness skin grafting with graft taken from opposite thigh with inguinal lymph node excision and biopsy taken. Lymph node with the appearance of cystic degeneration with hemorrhagic fluid aspirate was taken for cytological study. It was suggestive of superficial spreading melanoma of left foot pigmented lesion with a maximum size of 2.5 cm with lymphatic tumor emboli detected with no other signs of metastasis. An incisional biopsy of left inguinal lymph node was suggestive of metastatic melanoma of Clark level II. The patient was again planned for ilioinguinal block dissection with Sartorius cover in which approximate 7 × 7 × 6 cm of pelvic lymph node block dissection was done to achieve a tumor free surgical margin. It was followed up by the preservation of femoral artery, vein, and nerve with Sartorius cover. Histopathological diagnosis was suggestive of tumor abutting the superior and inferior margin and

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the base with margin free of tumor extension. Paraffin section report was suggestive of metastatic melanoma with maximum tumor size of 16.0 cm with tumor abutting the superior and inferior soft tissue margin and base. Revised superior and inferior margin were free of tumor extension with perinodal infiltration (1/4). This was followed up by post-operative radiotherapy.

## DISCUSSION

Melanomas are of neuroectodermal in origin, 20 times more commonly seen in whites than in blacks. Malignant melanoma is a rare occurrence in the Indian subcontinent with skin cancers amounting to 0.5-2/100,000 population, but due to a large population the number of cases encountered here is significant. Malignant melanoma is a serious skin malignancy with a bad prognosis, although early detection and excision and treatment give a better survival rate. Risk factors include sun exposure, ethnic factors and socio-economic factors, albinism, positive family history of skin malignancy, and other types of nonmalignant nevus.

Malignant melanomas were staged based on TNM Classification with revised classification listed below.

**Melanoma TNM classification<sup>1</sup>**

Tumor Classification	Thickness	Ulceration status/mitosis
Tis	NA	W/O ulceration and mitosis<1/mm <sup>2</sup> With ulceration and mitosis<1/mm <sup>2</sup>
T <sub>1</sub>	≤1.0 mm	W/O Ulceration With ulceration
T <sub>2</sub>	1.01-2.0 mm	W/O ulceration With ulceration
T <sub>3</sub>	2.01-4.0 mm	W/O ulceration With ulceration
T <sub>4</sub>	>4.0 mm	W/O ulceration With ulceration
Nodes classification	Number of metastatic nodes	Nodal metastatic mass
N <sub>0</sub>	0 nodes	N/A
N <sub>1</sub>	1 node	Micrometastasis Macrometastasis
N <sub>2</sub>	2-3 nodes	Micrometastasis Macrometastasis In transit without metastatic
N <sub>3</sub>	4 or more	Nodes

Primary tumor mitotic rate (histologically defined as the number of mitoses/mm<sup>2</sup>) is an important independent adverse predictor of survival. For T1 melanomas, a mitotic rate of at least 1 mitosis/mm<sup>2</sup> replaces Clark's level of invasion as a primary criterion for defining the subcategory

of T1b. The presence of ulceration remains an adverse predictor for survival.

The presence of nodal micrometastases can be defined using both hematoxylin and eosin (H and E) or immune histochemical staining.

## Diagnosis

Diagnosis of a melanoma is made by its ABCDE rule characterized by its asymmetry, border, color, diameter, and evolution in character of a melanoma. Diagnosis is based on full thickness excisional biopsy in mm (Breslow), level of invasion (Clark level I-V), presence of skin characteristics, and clearance of surgical margins.<sup>5</sup>

## Treatment Options

Surgery - a wide local excision of entire melanoma along with the surrounding healthy skin margin is cut off for prevention of a further recurrence. For *in situ* tumors, we generally treat by wide excision with skin margin of 0.5 cm with the use of imiquimod cream with or without radiation therapy. For tumors of Breslow thickness of 2 mm, we take a skin margin of 1 cm and 2 cm for tumors staged at IIb or beyond. This is associated with sentinel lymph node biopsy which if suggests cancer cells lymph node dissection is recommended. Sometimes in stage III or beyond adjuvant therapy such as radiotherapy, immunotherapy, targeted therapy, or chemotherapy may be considered.

Nonresectable-transit metastases or inoperable primary tumors of the limbs without additional metastases may be treated with isolated limb perfusion using, e.g., Melphalan and tumor necrosis factor or treatment can be only restricted to radiotherapy only. Palliative therapy for advanced disease with several metastases in different anatomical regions should initially use well tolerated single-agent cytotoxic drugs such as dacarbazine, as any systemic therapy did not result in survival prolongation but symptom palliation only. Fit patients with high volume visceral metastatic disease, who need rapid symptom palliation may be treated with combination chemotherapy in view of the superior response rates reported in some trials. Palliative radiotherapy should be considered especially for symptomatic brain or localized bone metastases only.

During melanoma follow-up, patients are clinically monitored to detect a relapse and to recognize additional skin tumors, especially a second melanoma, as early as possible. 8% of all melanoma patients develop a secondary melanoma within 2 years of their initial diagnosis. Melanoma patients also have increased risks for other skin tumors. In patients with lentigo maligna melanomas, 35% develop another cutaneous malignancy within 5 years.<sup>5</sup>

## CONCLUSION

The approach should be prognosis based. Patients with thin primary melanoma have only a small risk of melanoma and does not need a regular radiological investigation follow-up. However, in the case of thick primary melanomas CT/WHOLE BODY PET SCAN but there is no effective salvageable therapy available till date except early successful diagnosis of relapse and use of such patients in clinical trials.

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